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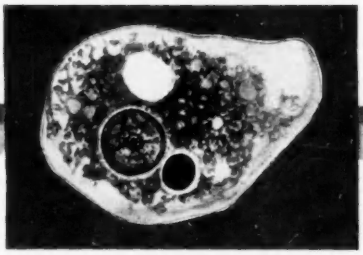

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1. Sodeman, W. A., and Beaver, P. C.: *Am. Jour. Med.*, 12:440, Apr., 1952.
2. Zavala, D. C., and Hamilton, H. E.: *Ann. Int. Med.*, 36:110, Jan., 1952.
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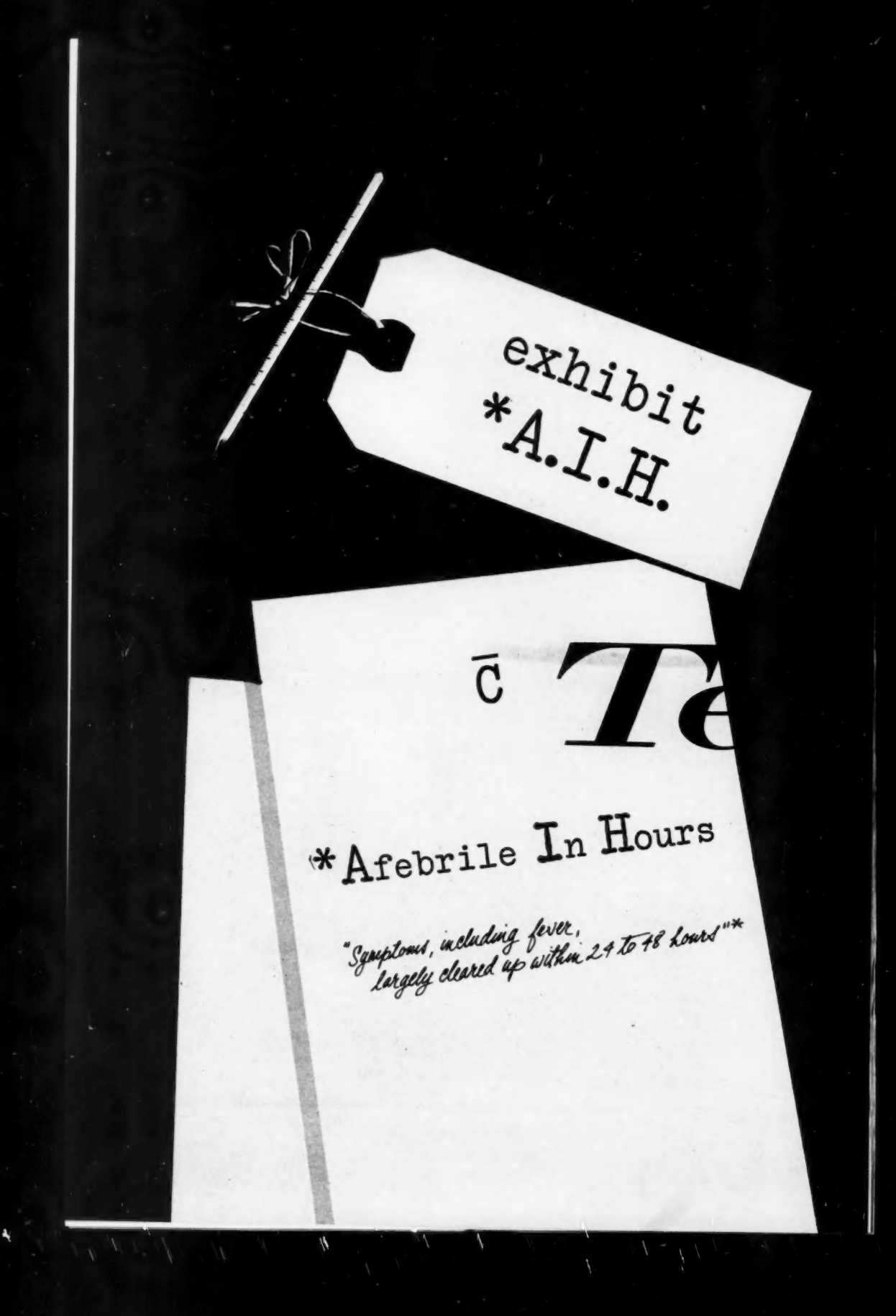
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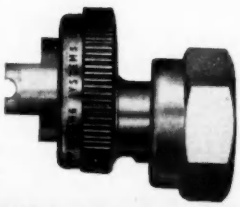

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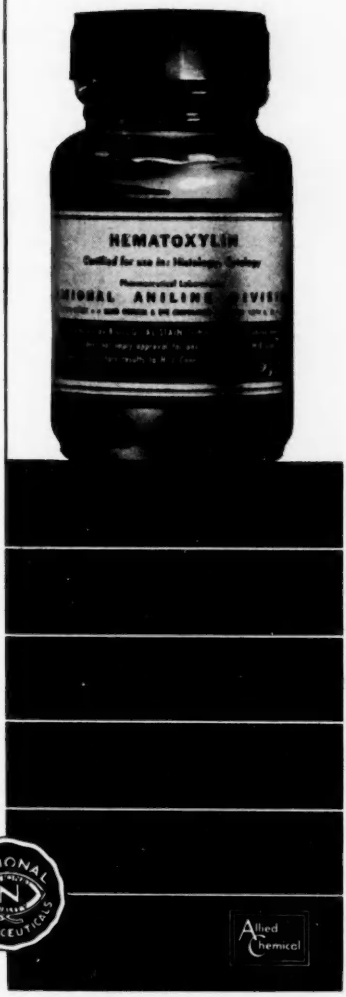

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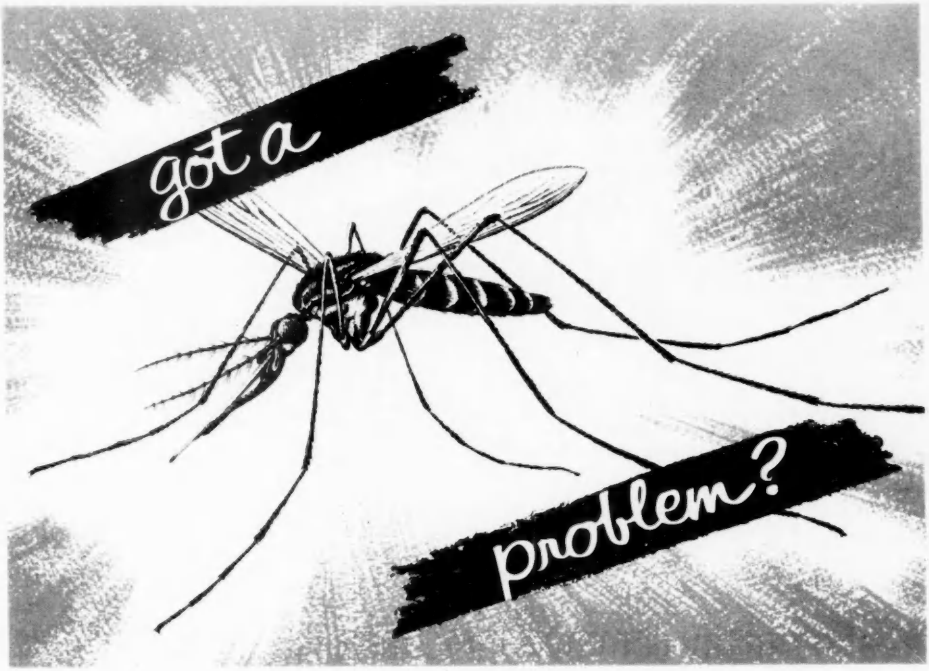

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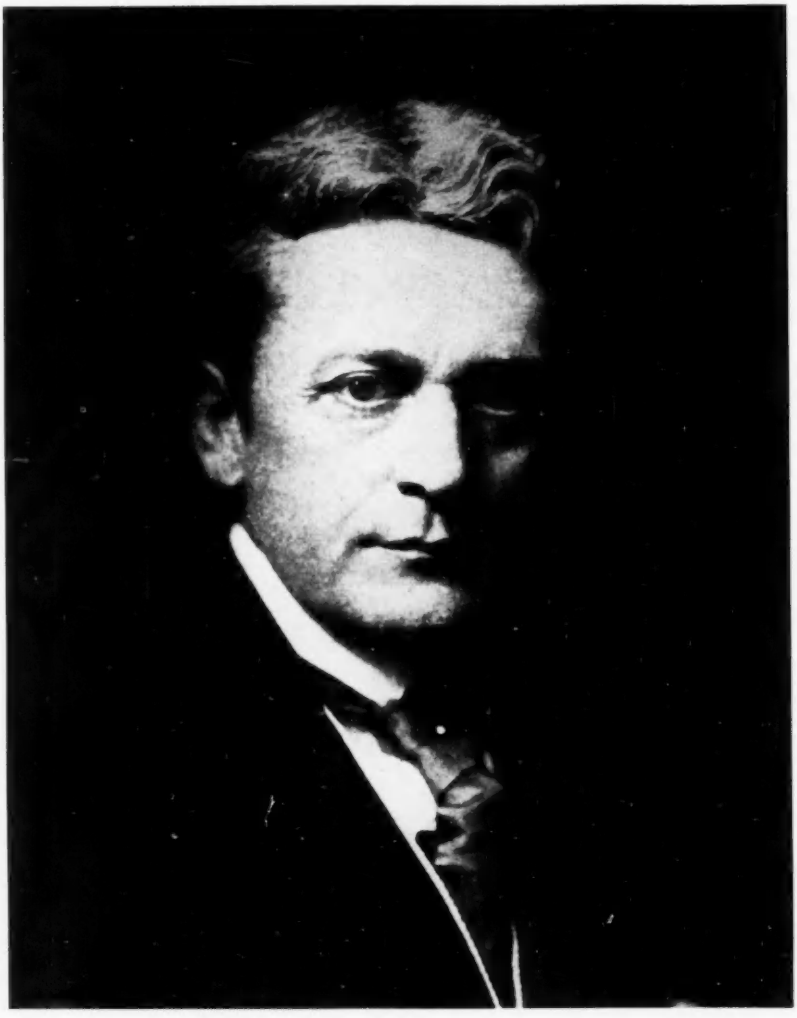

PLATE I. Thomas H. Fenton, Founder and First President of the American Society of Tropical Medicine.

A HALF CENTURY OF TROPICAL MEDICINE[1]

QUENTIN M. GEIMAN

Department of Tropical Public Health, Harvard School of Public Health, Boston, Mass.

The celebration of a fiftieth anniversary is an occasion for the examination of origins and achievements, and an attempt to set a course for the future. What has been prepared is an account of growing up and not just of growing old. Biographical sketches of the American Society of Tropical Medicine were written by the Society's secretary, Dr. John G. Swan, on the tenth anniversary (Swan, 1913) and by Dr. Ernest Carroll Faust on the fortieth anniversary of the Society (Faust, 1944). Repetition in part is necessary but an additional attempt will be made to present the background that led to the organization of a society of tropical medicine in this country, an account about some of the personalities involved in the early years of its existence and a summary of the notable achievements in medicine and public health on which to build the future of tropical medicine in America.

Information about the early years of the Society from 1903–1921 was obtained from the original Minutes Book of the Society (Fig. 1). Since the early correspondence files were not available for reference, I was fortunate enough to obtain in the library of the Harvard Medical School copies of the transactions, with few exceptions, that were originally in the personal library of Dr. Richard P. Strong. Additional information was obtained from the official publications of the Society including the American Journal of Tropical Diseases and Preventive Medicine published in three volumes from 1913–1916 and from the American Journal of Tropical Medicine initially published in 1921.

Interpretation of the available records is entirely personal and there are, no doubt, many omissions, for which an apology is made. Any supplementary information volunteered by members, including letters, anecdotes or pictures that are not recorded in Society publications should be collected and preserved in the archives of the Society for future reference.

To reconstruct the times in which the initiators of the American Society of Tropical Medicine lived, one asks questions about the nature of news items at the turn of the century, about the current state of medicine and science at that time, about new discoveries in tropical medicine and something about communications and travel that disseminated information and brought peoples from different parts of the world together. Joseph Needham (1943) has said "a scientific worker is necessarily a child of his time and inheritor of the thought of many generations". We might paraphrase that quotation to read "a scientific organization is necessarily the child of its time and inheritor of the thought of many generations".

In copies of the World Almanac and Encyclopedia, medical journals and news-

[1] Presented Nov. 12, 1953 at the fiftieth anniversary dinner during the annual meeting of the American Society of Tropical Medicine and Hygiene in Louisville, Kentucky.

FIG. 1. A photograph of the original minutes book of the American Society of Tropical Medicine.

papers from 1902–1905 the following pertinent facts and events are recorded. The population of this country was estimated on January 1, 1903 to be seventy-nine million, eight hundred thousand. Madame Curie discovered radium in 1903. Nineteen thousand automobiles were produced in that year with approximately fifty thousand in operation in the whole country. The automobile record for speed was fifteen miles in 14.21 minutes. An electric automobile made the distance of 244 miles from Boston to New York in twenty-two hours, fifty-two minutes of running time. An automobile starting from San Francisco required sixty-four days to reach New York City. In comparison, ships were relatively fast, because the record of sailing time from New York City to London was five

days, 8 hours, 16 minutes. Only sporadic information appeared in the papers about the flying of heavier-than-air craft and popular acceptance of the possibility of air travel did not begin until 1908. In terms of communications we had telephones and cables, but we should note that the first wireless message was sent across the Atlantic by Marconi in 1902 from Glace Bay, Nova Scotia.

The medical problems concerned with the Spanish-American War and the involvement of armed forces in tropical areas, the political events having to do with Cuba, the death of Walter Reed on November 22, 1902 and the award of the second Nobel prize in medicine to Ronald Ross for his outstanding contributions to our knowledge of malaria, all focused attention on tropical medicine.

To retrace our steps to the local situation in Philadelphia during the close of 1902 and the beginning of 1903, the Journal of the American Medical Association contained numerous papers on yellow fever and editorials on hookworm disease, trypanosome disease and cosmopolitan diseases of the tropics. We should recall that this was the time during which many outstanding discoveries were made in medical parasitology and in tropical medicine. Charles Wardell Stiles (Stiles, 1903) and Bailey K. Ashford (Ashford, 1911) uncovered the extent of hookworm disease in our southern states and a new species of hookworm was described. The causative agents of African sleeping sickness, of leishmaniasis, of syphilis were discovered and Schaudinn made a morphological distinction between the ameba that causes dysentery and the nonpathogenic *Entamoeba coli*. It is not surprising then to find that a course of lectures on tropical diseases was scheduled by Jefferson Medical College during the early winter of 1902 and 1903. This series of lectures was advertised as the first of its kind to be held in the United States and they were given by Captain Charles F. Kieffer, Assistant Surgeon of the United States Army (Kieffer, 1903). Instead of the twenty individuals expected at these lectures, approximately one hundred fifty attended. In referring to Captain Kieffer's lectures, we find that he considered malaria, yellow fever and plague too local and thoroughly understood to be included in the lectures, because these diseases received adequate attention in the medical schools of that day. The subjects chosen for discussion included dysentery, hill diarrhea, epidemic gangrenous rectitis, abscess of the liver, filariasis, diseases caused by intestinal parasites, beri beri, special tropical fevers and skin diseases, frambesia, tropical granulomata and hygiene. These lectures were published promptly in the Philadelphia Medical Journal, a journal which also contained numerous articles from time to time on malaria, yellow fever, plague, dengue, and dysentery.

Whether or not the University of Pennsylvania Medical School did not wish to be outdistanced by Jefferson Medical College, the Society records show that Dr. Thomas H. Fenton wrote a letter to prominent physicians in Philadelphia on January 29, 1903, in which he raised the question of the organization of a society concerned with tropical diseases.

"Dear Doctor—As is well known, there are many areas within the United States proper which are subtropical, and the new possessions of our country are almost wholly tropical. This would seem to make it necessary that the profession should give closer attention, per-

haps, to what are considered tropical diseases. It will certainly be admitted that in a center of medical education like Philadelphia, there should be opportunity afforded for this kind of study. This view is confirmed by the recent establishment in this city of a series of lectures on 'Tropical Diseases.' I have thought for a long time that the existence of a society, at the meetings of which these topics would be considered, would perhaps act as a stimulus to the promotion of these studies, and favor the development and increase of our knowledge in this particular direction. All to whom I have spoken are heartily in accord with the proposal, and seem, furthermore, willing to join such an organization. The society need not be a large one nor involve, by frequent meetings, too much tax upon the time of a busy practitioner. If you incline favorably to the view expressed, I shall be glad to have you meet a few physicians at my house Monday evening, February 2nd, at 8:15, for the purpose of discussing the expediency of forming such a society.

Very truly yours,
Thos. H. Fenton."

"Dear Doctor:

At an informal meeting held Feb. 2nd, the question of forming in this city a society for the study of Tropical Diseases was favorably considered. The consensus of opinion of those present and of a number who had sent letters in response to the call, was, that the time is ripe for the formation of such a society in Phila., somewhat on the following lines. The membership should be somewhat restricted in numbers and should include a list of honorary and corresponding members, the dues should be merely nominal and the number of meetings confined to three or four yearly. If you incline favorably to this view, the undersigned Committee will be glad to have you attend a meeting for the further consideration of the subject on Monday, March 9th, at 8:30 P.M., at 1319 Spruce St.

Thomas H. Fenton
Sec."

The recipients of the first letter were asked to meet with him at his house, Monday evening, February 2, 1903. An informal meeting was held on that date at which time proposals for an organization of a society of tropical medicine were considered. The name of the organization was to be the Society of Tropical Medicine of Philadelphia. A committee was appointed and the second letter, under the date of February 28, 1903, calling a meeting on March 9 at Dr. Fenton's office, was sent to those who were interested. At that meeting the society was organized, officers were elected and a favorable vote was taken to retain the name previously decided upon. However, on March 21 the Council met at the Art Club in Philadelphia and the name of the organization was changed to the American Society of Tropical Medicine.

It is quite interesting to note that an editorial entitled "Tropical Medicine" appeared in the Journal of the American Medical Association dated March 21, 1903. In that editorial, such statements about tropical medicine as the following are included—". . . more importance with each year, both to the profession and the public", ". . . little has been done so far as treating the subject as a specialty is concerned, though we owe some of the best conducted and most valuable investigations to our own countrymen". This editorial ended with the sentence "Tropical medicine, however, cannot well be overlooked in any future program of the association." Now we have already mentioned the official organization of the American Society of Tropical Medicine on March 9. This coincidence emphasizes that the newspaper, scientific and medical articles about

malaria, yellow fever, plague, hookworm disease and dysentery placed the subject of tropical medicine in sharp focus and the medical profession of this country was becoming aroused to the need for a national and not just a local organization concerned with tropical medicine.

Before passing on to events of the first ten years of the Society's existence, a tribute at this fiftieth anniversary celebration needs to be paid to Dr. Thomas H. Fenton, who founded the Society (Plate I). Through the courtesy of the Philadelphia County Medical Society, a photograph of Dr. Fenton was obtained for preservation in the archives of the Society. Dr. Fenton was a widely known eye specialist of Philadelphia and lived at his home, 1319 Spruce Street, where the initial meeting of the Society was held. Dr. Fenton died at the age of seventy-two after a long life of successful practice and teaching of medicine. He specialized in physiology and pathology of the eye and became an authority in that field of medicine. He was associated with at least six hospitals and was a Fellow of the College of Physicians. Dr. Fenton was the past president of the Philadelphia County Society and, as we know, the past president and dynamic leader of the American Society of Tropical Medicine through the first years of its existence. Evidence of his broad community interests were membership in civic, fraternal and social clubs including the Art Club of Philadelphia, Philadelphia Board of Education, Athletic Club, Union League, and life membership of the Academy of Natural Sciences of Philadelphia.

Another staunch member who needs to be singled out for a tribute is Dr. John G. Swan (Plate II). Dr. Swan served as assistant secretary of the Society for four years and then as secretary from 1907 to 1918. Many years of service were given by Dr. Swan to the Society. In fact, the first minutes were written by him (Fig. 2) even though he was assistant secretary, with Dr. Joseph McFarland as secretary. Proof of Dr. Swan's conscientious discharge of his duties with a keen sense of humor is to be found in a number of letters written by him to Dr. Richard P. Strong about Society affairs and the annual meeting at the time that Dr. Strong was president in 1913–1914. These letters show that Dr. Swan was beset by the worries of all secretaries including affairs about the finances, about papers submitted for the program, attendance at the annual meeting, and the genuine progress of the Society. Dr. Swan continued his duties when he moved to Rochester, but eventually relinquished them when the Society made him its vice-president (1919) and then its president in 1920. Dr. Swan knew the earlier history of the Society intimately and reviewed its progress during the first ten years in his Secretary's Report (Swan, 1913) given at the annual meeting in 1913 at Philadelphia. Dr. Swan was assigned to Base Hospital 19, which he organized for duty in France during World War I with the rank of Lieutenant Colonel. He was cited "for exceptionally meritorious and conspicuous service". In 1919, after separation from the Army, he was appointed a Red Cross Commissioner to the Dominican Republic to study health problems and make recommendations for their improvement to the National Red Cross. After this assignment, he entered energetically into the medical battle against cancer, serving as executive secretary of the New York State Committee of the American Society for the

PLATE II. John Mumford Swan, Assistant Secretary and Secretary of the American Society of Tropical Medicine from 1903 to 1918.

Control of Cancer, now known as the American Cancer Society. Dr. Swan died at the age of 79 years in November, 1949, and the Society owes him much for his faithful service from the time of its organization to his death.[2]

[2] Information obtained through the courtesy of the Rochester Academy of Medicine, Rochester, N. Y. Photograph obtained through the courtesy of the Armed Forces Medical Library, Washington, D. C.

A meeting was held at 1319 Spruce St.
March 9, 1903 for the formation of a society
in Philadelphia for the Study of Tropical Diseases.
Dr. Roland G. Curtin was elected chairman
and Dr. Thomas H. Fenton, secretary. There
were present Drs. Wm. Pepper, W. P. A. (Retired)
McCarthy, Gleason, Kieffer, Shoemaker,
Hare, J. M. Anders, McFarland, Hewitt,
Wilson, Kyle, Stahl, Curtin, Wadsworth
and Fenton. Com
Communications were read from Drs.
Daland, Neugle, Wasser, Percival, Lloyd,
Dickler, Mitchell, Keen, Randall, J.
Madison Taylor, J. Chalmers DaCosta,
Coplin, Montgomery, V. Solis Cohen, S. D.
Risley, Dixon, James B. Walker, Caspar
Morris, Stelwagon, de Schweinitz, Fluhrer,
Henry, Schaeffer and Hopkins either sig-
nifying their intention of being present
or their cordial cooperation with the purpose
of the meeting.
A copy of the circular letter sent out by Dr.
Fenton under date of January 29, 1903 was read
and also a copy of the communication of Feb-
ruary 28, 1903, signed by the following com-
mittee: Wharton Dickler, James M. Anders,
Judson Daland, Joseph McFarland, James
C. Wilson and Thomas H. Fenton.

FIG. 2. A photograph of the first page of the Minutes Book, describing the initial meeting of the American Society of Tropical Medicine.

During these early years of the Society, the building of the Panama Canal was a major news item. The United States took over the canal in May, 1904, and soon thereafter, three representatives of the Society, Drs. A. Egbert, J. McFarland, and R. G. Curtin, visited the Canal Zone. Their published reports (Egbert, 1905; McFarland, 1905; Curtin, 1905) provide an interesting background for the accomplishments that were to follow as a result of the outstanding ability of Dr. W. C. Gorgas. Since the Society was attempting to build prestige by getting prominent speakers and electing outstanding honorary members, such as Sir Patrick Manson, Drs. Ronald G. Ross, Aristides Agramonte, George H. Nuttall, William H. Welch, Simon Flexner, and Professor Kitasato, we find that two papers were presented by Dr. Gorgas before the Society on December 8, 1905, and March 24, 1906. On June 11, 1910, Dr. Gorgas, as president of the

Society, spoke on "The Expenses Necessary for Sanitation in the Tropics" (Gorgas, 1910). From this address one can discover the extraordinary administrative ability and vision of Dr. Gorgas and his final paragraph was a prophecy that has come true. "We therefore believe sanitary work in the isthmus will demonstrate to the world that the white man can live and work in any part of the tropics and maintain good health and that the settling of the tropics by the Caucasian will date from the completion of the Panama Canal."

Numerous other members stand out for their contributions during the early years of the Society's existence. Dr. William S. Thayer, one of the original members of the organization, became president in 1911 and in his Presidential Address (Thayer, 1911) chose to set forth the purposes and functions of the Society in matters of membership and in public and educational influence concerned with the control of disease. He expressed his regrets that so few clinicians from other parts of the country were members, because of the belief that the organization was a local society composed of members from Eastern cities. He then, in his characteristic constructive manner, proceeded to suggest placing members on the Honorary list whose membership had lasted more than a certain number of years, that the limited membership should not be overburdened by nonproductive associates and that the Society should drop "from the list of membership such persons as shall have been absent from say three consecutive meetings of the Society without proper excuse, or who shall have failed to produce a piece of medical research within a given period of years." Apparently the questions raised were considered by the Council and it was agreed that "only such candidates for membership shall be considered as had published work of real value in the field of tropical medicine or who through other special attainments or position are peculiarly fitted to give valuable counsel to the organization . . . and that every applicant for membership should be proposed by two members. . . ." Dr. Thayer proposed to make the Society a more homogeneous, representative and useful organization. Since Dr. Thayer was a key figure in the American Medical Association, he felt keenly that the American Society of Tropical Medicine should render real public service and asked why the Society had done so little with prophylaxis against malaria fever. To quote his words, "When we look at what has been done in Italy, Suez, many points in India and Africa and in Panama and then turn to the article by Dr. Howard in Ross' recent book on the prophylaxis of malaria we may well hide our heads for shame. There has been scarcely a single public measure taken in the most malarious districts of America to save the hundreds of lives that are being sacrificed yearly. We sit with folded hands and wait for some one else to take the initiative. Why should we not, as a body, appoint a committee to make a complete report as to those measures which might be at most practical, and easy of adoption, in different parts of this country? . . . a report that might set the matter clearly before government, city, county, and town officials." He proceeded to say how this could be done and one wonders whether the sowing of this seed had anything to do with the subsequent increased interest in malaria and formation of the National Malaria Committee in 1916. Dr. Thayer in this address was still not finished. He raised a question

about measures to be taken against the possible entrance and spread of bubonic plague. He also raised the question about organizing a congress of tropical medicine in 1915 when the Panama Canal was to be formally opened. He believed that negotiations should be undertaken immediately and that the organization of such a congress should be arranged in connection with the International Society of Tropical Medicine.

This straight speaking from Dr. Thayer led to greater national activity and interest in public affairs, but the organization was not thinking in terms of national service to judge by the meager recorded activities during World War I. To be sure World War I was not fought in subtropical or tropical areas, but only a few news notes about diseases in Europe appeared in the Journal. When the influenza epidemic of 1918 cancelled the annual meeting, interest sank to a new low and it was not until the year of 1920 that the Society began to function more actively.

In retrospect, the difficulties through these early years of existence apparently had to do with the lack of an official publication as an outlet for notices about Society affairs and the publication of papers in the field of tropical medicine. In 1913 the American Journal of Tropical Diseases and Preventive Medicine became the official publication of the American Society of Tropical Medicine with Dr. Creighton Wellman as editor-in-chief. This Journal lasted only through three volumes. Then there was another interval during which time the earlier method of publishing the transactions as a separate volume was continued. In 1920, President Henry J. Nichols devoted his address to remarks about the state of affairs in the Society (Nichols, 1921). He stated that he began to feel that his only function was to conduct a post-mortem but that "it is evident that the patient is making a good recovery from the depressing influence of war and pestilence, and, like other convalescents, is undergoing a rebound to a better state of health than ever." Through the energetic initiative of President Nichols, arrangements were made with the Williams & Wilkins Company to found a new publication entitled THE AMERICAN JOURNAL OF TROPICAL MEDICINE. This journal began its existence in January, 1921 and if membership is an indicator of the Society's growth, the acquisition of an official publication was responsible for a continuous upward climb in membership from approximately 120 to over 1300 in 1945. There were difficult years in financing this publication, but the patience of the publishers and individual solicitation of support by the second editor, Col. Charles Franklin Craig, helped to provide for its continuity up to the time of his death. The contributions of Col. Craig to tropical medicine and to the Society were vast. A testimonial was presented to him in 1946 and we are greatly indebted to Dr. C. C. Bass for a memorable Charles Franklin Craig Lecture in 1951 (Bass, 1952) that will preserve the accomplishments of Col. Craig for posterity. The annual meeting in 1951 was scheduled for San Antonio to honor Col. Craig and his work, but death intervened.

The inflated membership which resulted from World War II carried the Society through to amalgamation, when we started anew with Volume 1 of our present official American Journal of Tropical Medicine and Hygiene. The Society

should be grateful for the efforts of its series of editors and at the present time our Journal is enjoying a most successful existence under the skillful guidance of Dr. Lewis W. Hackett and his editorial committee.

The Society had been affiliated for a number of years with the American Association for the Advancement of Science, and at the meeting of Section N (Medicine) in December, 1940, several members of the Society contributed to a Symposium on Human Malaria which was published in 1941 (Boyd *et al.*, 1941).

In strong contrast to the lack of Society activities in World War I, an entirely different record was made during World War II. The Society had also been affiliated with the National Research Council. Anticipating our involvement in war in the tropics, the Division of Medical Sciences of the National Research Council appointed a Subcommittee on Tropical Diseases which held its first meeting in May, 1940, with Dr. Wilbur A. Sawyer as chairman. Dr. Henry E. Meleney succeeded Dr. Sawyer in January 1941. The first activity of the subcommittee was the preparation of directives for the Army Medical Corps on the diagnosis and treatment of tropical diseases. In the spring of 1941 the subcommittee assisted the Army Medical School in starting a short course in tropical medicine which was repeated many times during the war, and was attended not only by hundreds of army medical officers but also by scores of civilian instructors from medical schools. Several members of the Society participated in directing and teaching this course. In August, 1941, funds became available to the National Research Council for research and the subcommittee stimulated and sponsored about fifty projects on a wide range of tropical diseases and their prevention, many of which were conducted by members of the Society. Another project in which members of the Society cooperated with the National Research Council, the Association of American Medical Colleges and the Markle Foundation was providing opportunities for instructors from medical schools to attend short courses in tropical medicine at the Army Medical School or Tulane University, and to gain practical experience at hospitals in Central America. A report of all of these activities was given by Dr. Meleney to the Society at its meeting in 1944 (Meleney, 1945; 1953).

I believe that the Society can be justly proud of the record of this committee because with few exceptions each member of the American Society of Tropical Medicine and the National Malaria Society took part in the recommended broad activities that involved control measures in war areas, laboratory research and teaching in the Armed Forces and in our medical schools and schools of public health. Here is an example of how a group of professional men, interested in a specialty and with the stimulus of war, can be of service to their country and in a short space of time advance knowledge in a way that would require many generations in peacetime.

The members of the Society formed the nucleus for the program of urgent expansion in the field of tropical medicine, and clinicians and scientists responded by increasing membership to a maximum of 1309 in 1945. In 1944 the Secretary listed 521 members of the Society in the Armed Forces. The wartime efforts of our members also had international influence because it led to coordinated pro-

grams of effort with our allies, providing an excellent foundation for the international aspects of applied tropical medicine that have been initiated and carried out by the World Health Organization since 1948.

AMALGAMATION

At the annual meeting of the Society in July, 1912, Dr. J. H. White in his President's Address spoke on "The Eradication of Malaria". This paper, as was that of Dr. Thayer, was a call for Society action to support malaria control. One sentence in his address, "The actual work of eradication of malaria is elemental in its simplicity, but calls for untiring watchfulness and absolute thoroughness" is an amazing understatement.

At the annual meeting of the Society in May of 1916, a paper by Dr. Frederick L. Hoffman, was presented under the title "A Plea for a National Committee on the Eradication of Malaria". The energy and forcefulness of Dr. Hoffman led to the formation of the National Malaria Committee in 1916 on the same day that this paper was read. This Committee carried on its outstanding activities for twenty-five years until 1941 when a new constitution was adopted and its name was changed to The National Malaria Society. I need not go into the activities of this organization at this time because that has been done thoroughly by Boyd (Boyd, 1943), Hinman (Hinman, 1949) and Andrews (Andrews, 1951).

The close association of the American Society of Tropical Medicine with the National Malaria Society started in 1931. Through the subsequent years these two organizations scheduled joint annual meetings and the two societies had many activities, aims, and achievements in common. The possibility of joining forces was often considered by the officers and councillors of the two organizations. On August 17, 1950, Dr. Mark F. Boyd, who had been associated with the National Malaria Committee from its start and its secretary from 1930 through 1946, who was extremely active in the affairs of the American Society of Tropical Medicine and who was editor of its Journal from 1947, took the initiative to write the Secretary-Treasurer of the American Society of Tropical Medicine suggesting that amalgamation of the two organizations be considered. A copy of this letter follows:

August 17, 1950

My dear Dr. Geiman:

The possibility of the amalgamation of the National Malaria Society with the American Society of Tropical Medicine, has been discussed intermittently in certain circles for nearly two decades. As long as malaria continued as an important public health problem in the United States, this idea did not make much headway, as the malaria group was quite cohesive, and subsequent to the reorganization of the National Malaria Committee as the National Malaria Society, with the development of a Journal of its own, it was able to stand solidly on its own feet, and has occupied a thoroughly sound financial position. On the occasions when the possibility of such a fusion has been discussed, so far as I am aware, it has always been in ASTM circles, but it appeared that initiative for such a move was expected to arise in the NMS. For the reasons above expressed, the NMS have, of recent years, been increasingly concerned with the future of their society, and have discussed various possible changes. It consequently appears to me that the time is propitious for the officers and members of the ASTM to approach the officers and members of the NMS to see whether

an acceptable basis for amalgamation of the two organizations may be effected. Consequently I wish to request that this communication be laid before the members of the council and that they authorize you to approach the officers of the NMS on the subject.

It would appear to me that consideration of the following topics, with action more or less along the lines indicated would be necessary:

1) The incorporation of all members of the NMS in the ASTM, and the amending of the membership qualifications of the ASTM to permit the future election of persons having present NMS qualifications. I believe that at present there are approximately 200 persons who are members of both organizations.

2) Continue dues in the amalgamated organizations at the ASTM level.

3) The meetings of the fused organization to provide a minimum of two half days sessions with a program arranged with special reference to the interest of those occupied with malaria or other arthropod-borne infections. Such sessions may be held simultaneously or concurrently with other ASTM sessions, rather than consecutively.

4) Incorporation of the Journal of the NMS with the AJTM, with a title reading

American Journal of Tropical Medicine
Incorporating the
Journal of the National Malaria
Society

5) That the enlarged journal appear monthly, to form an annual volume of a minimum of 800 pages.

6) That the publication funds of the NMS at the time of the amalgamation be expended in defraying all or part of the publication cost of lengthy papers (in excess of 20 pages of script) dealing with malaria or other arthropod-borne infections.

Other topics might require discussion, but I believe that the above are the most important.

Should this proposal appeal to the council of the ASTM, I wish to request that they take early action, so that overtures may be made officially at the Savannah conjoint meetings. While formal proposal would necessarily require an invitation from the ASTM membership to that of the NMS, the matter could be expedited if the officers of the NMS were advised in advance that the ASTM has such a proposal under consideration.

At any rate, it is my personal opinion that whatever chance there may be for such amalgamation, will require the initiative of the ASTM, rather than to expect that it will be petitioned for by the NMS.

Cordially yours,
Mark F. Boyd

This letter was circulated among the officers and councillors of the two organizations and it was agreed that the time was ripe for amalgamation. The officers and councillors of the two organizations were requested to come prepared to discuss the matter at the joint annual meeting in Savannah, Georgia. The presidents of the two organizations appointed representatives to a joint committee to explore the possibilities and details of amalgamation thoroughly and make recommendations for presentation and vote to the members of the two societies. This joint committee was composed of Justin Andrews, S. W. Simmons, Martin D. Young, and Jack Henderson of the National Malaria Society; Paul Russell, Quentin M. Geiman, Donald L. Augustine, and William A. Sodeman of the American Society of Tropical Medicine. During the year G. Robert Coatney and Hamilton Anderson were appointed as alternates. This committee, through subcommittee action, drafted a new constitution, decided on Journal policies and publishing agreements, explored the legal and financial aspects of

amalgamation and made the appropriate recommendations for consideration of the two societies. The proposed constitution was sent to members of the two societies requesting a vote on the amalgamation, acceptance of the constitution and the continuation of the Tropical Medicine News. No serious objections were raised by the members of the American Society of Tropical Medicine except for one active member, and the amalgamation, the constitution and by-laws were approved. Since the result of the vote of both societies was practically unanimous, proceedings for the official amalgamation at the annual meetings in Chicago were prepared. Subsequently, at the annual meeting in Chicago, 1951, the National Malaria Society officially and legally dissolved itself, being a private organization; but to avoid legal complications and because of the one dissenting voice, the American Society of Tropical Medicine had to be dissolved legally.

A meeting to organize the new American Society of Tropical Medicine and Hygiene was scheduled for the morning of November 17 at the Congress Hotel in Chicago. I am not going to go into the details of that meeting because they can be found in the transactions of the annual meeting published in the American Journal of Tropical Medicine and Hygiene for September, 1952, but it is a pleasure to recall the smooth precision of that meeting after the hard work and misgivings of the preceding months. Immediately after the organization meeting, proceedings were set in motion to incorporate the new American Society of Tropical Medicine and Hygiene in the State of Delaware. Incorporation was effected on January 21, 1952, giving the Society legal status to begin transacting its affairs. The legal machinery for the dissolution of the old Society, however, required time because of the settling of bills and affairs involved with the publication of the Journal, preparation of the petition for dissolution to the Court and getting the petition on the Court Docket. The official date of dissolution in the Courts of Philadelphia was April 9, 1953.

After official organization and incorporation, an immediate dilemma of the new organization had to do with obtaining a publisher for its Journal. Negotiatiations were started with the Williams & Wilkins Company in Baltimore to draft an entirely new publishing agreement that was acceptable to the Williams & Wilkins Company and to the officers and councillors of the new Society. A satisfactory and equitable agreement was finally agreed upon and settled on January 31, 1952. The editor, Dr. Lewis Hackett, has edited the new Journal and guided its finances most satisfactorily under the new publishing agreement. Under the terms of this agreement, the Journal can now be operated as an asset instead of a liability to the Society.

The amalgamation as carried out and the success of the Society under its new name, with a new constitution, new publishing agreement and large membership is ample evidence that we have a strong organization that has grown up and come into its own. This new Society has been able by this procedure to start over again and shed the traditions that were becoming problems in the two parent organizations. We can now plot our course and our program according to the needs of the times and plan a program of future activity that will maintain the Society as a strong organization and provide community, national

and international services. Our interests are no longer limited to tropical medicine, but to a field of broader importance, the field of tropical public health. The new Society is no longer confined solely to clinical tropical medicine, but it is a society for the purpose of advancement of tropical medicine and hygiene which includes medicine, nursing, engineering, entomology, parasitology and related specialties in this field. To treat successfully a single patient today, control diseases and advance the public health, the clinician needs the support of the organic chemist, pharmacologist, the research worker, the engineer and skilled public health workers.

The challenge for future activities becomes quite clear. We have grown up through fifty years of turbulent world affairs. The Society's publications had served as an outlet for field research and its international activities; the Society that played a minor role in World War I, grew up to play an extremely important role in World War II and in the recent Korean episode. The Society has served and assisted in international activities such as the Fourth International Congress in Tropical Medicine and Malaria in 1948 and in the World Health Organization. An organization is only as strong as its members and its inherited responsibility is to devise long range plans to maintain the level of activities and prestige which we now enjoy.

The impact of the vast increase in fundamental knowledge about diseases and their control in the tropics as a result of wartime activities and research is still being digested for practical application in the field. Throughout the seventeenth to the nineteenth century, the very existence of mankind seemed to be threatened by epidemics of infectious diseases that could not be controlled. Now we are confronted with the paradox that man himself is living longer because of the development of sulfonamides, insecticides, antimalarial drugs, antibiotics, improved methods of sanitation, improved economic conditions, thus creating a population stress in many parts of the world that threatens to become the primary problem and displace disease as man's worst enemy.

The optimism and foresight of Dr. Paul Russell in his Presidential Address of 1951 (Russell, 1952) might well serve as a foundation on which to build future activities of the Society.

"Man, who has so brilliantly devised measures for restraining death, may be expected to have similar success in regulating birth. . . . Let us lead the way with balanced medical and health care programs, designed for sustained public welfare."

Under a new name and a new constitution that is flexible we can plot our course, we hope wisely, so that the members of this organization fifty years hence can point with equal pride to the accomplishments of the second half century when compared with what was achieved during the first fifty years of its existence.

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ECONOMIC INTEREST IN TROPICAL MEDICINE

STACY MAY[1]

When it was suggested that I speak to this distinguished group, I accepted the assignment with great diffidence. For many years I have had a strong belief in the fruitfulness of cross fertilization between the several fields of learning, and it seemed logical that even so inexact and fumbling a discipline as economics should be able to contribute something of use and value to a group such as this whose concentration has focused upon carrying the findings of medical science to the great task of controlling disease in tropical areas.

My misgivings stemmed from the realization that my knowledge of tropical medicine was so scant that—if I may employ a vulgar phrase that may be meaningful to your craft—if put into one's eye it might or might not be sufficient to induce an acute conjunctivitis.

As I have tried, in the far too brief time available, to repair my ignorance sufficiently to allow me to sort out the economic factors with which I had some familiarity in a fashion that might make them relevant to the field of your interest, my diffidence has been far from dispelled, but my initial despair has been replaced by at least a moderate and qualified degree of hopefulness. For over the past six or seven years I have been working rather intensively upon the economics of the so-called underdeveloped areas of the Free World, and even the superficial reading that I have been able to do in your field has convinced me that, in its current usage, the term tropical medicine is essentially synonymous with the health problems of the underdeveloped areas.

Let me cite briefly the evidence for this conclusion.

I

The economists' definition of free world underdeveloped areas

When economists talk about the underdeveloped areas of the Free World, they are referring to those areas, free of the domination of Soviet imperialism, the economies of which are still relatively unaffected by the economic developments that generally are thought of as characterizing the industrial revolution of the 19th and 20th centuries. Realistically, of course, almost no peoples in the world today are untouched by modern industrial progress, but there is still a wide disparity in the degree to which industrial organization has taken root in such countries as the United States and Canada, Western Europe generally, Japan, Southern Australia, New Zealand, and South Africa compared with its incidence in almost all of the remainder of the Free World. To the economist, the underdeveloped areas of the Free World embrace the relatively unindustrialized lands occupied by more than one billion persons, including most of the expanse of Latin America, Africa, the Middle East, South Asia, Southeast Asia and Oceania.

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The economist is aware, of course, that no set of generalizations can be made that will apply accurately to the widely divergent peoples, cultures, economies, religions, climates, topographies, living standards, values, political outlooks and social aspirations either of the billion human beings that he arbitrarily classifies as falling within the underdeveloped areas, or of the half-billion that live in the countries that he denominates as industrialized. Despite the wide divergencies within each category, he has found sufficient contrast between the general economic status of those who live within the one and the other, to justify certain broad generalizations that are useful to his work.

Thus he has noted that, in 1949, income in the underdeveloped areas averaged about $80 per capita as against $473 for Western Europe and $1,453 in the United States; that the underdeveloped countries, on average, provided their peoples with one-third less food, when measured in calories, than did the industrialized nations, and that generally the disparity was even greater when measured by protein content; that they provided each inhabitant with only one-fourth as much cloth, with the services of one-sixth as many doctors, one-half as many teachers, and one-twentieth of the mechanical energy service. Their average incomes are one-tenth as high, their life expectancy one-half as long and their literacy rate one-fourth as high.

The geographer's definition of the tropics

When the economist turns to the geographer for orientation, he cannot fail to be impressed by the remarkable coincidence between his own demarcation of Free World underdeveloped areas, and the geographer's definition of the tropics. The latter's classification of tropical rain forest areas, tropical savanna, and tropical or subtropical steppe or desert areas when charted on the map includes all of Latin America except the extreme south, the same for Africa, most of the Middle East, South Asia and Southeast Asia, and most of the Pacific islands including a large part of Australia.

The greatest discrepancy between the geographer's tropics and the economist's underdeveloped areas is to be found in Northern Asia, a large part of which is now within the Communist orbit. But the area of coincidence is sufficiently striking to have generated a great amount of scholarly speculation, voluminous if inconclusive, as to whether or not there is a causal relationship between a tropical environment and meager economic progress.

The medical definition of tropical diseases

To what geographical areas does the medical authority refer when he speaks of tropical diseases? At this point, my diffidence closes in upon me again, particularly when I am addressing an audience such as this.

From my meager reading of your literature, I gather that tropical medicine is concerned primarily with the prevention and treatment of the so-called mass diseases, such as:

1. Malaria, bilharziasis, yaws, hookworm, tuberculosis, trachoma, and a large variety of gastro-intestinal ailments;

2. A variety of pestilential diseases that are mass diseases in epidemic form—such as cholera, smallpox, bubonic plague, typhus, typhoid and yellow fever; and

3. Nutritional diseases—such as beri-beri, pellagra, scurvy, rickets, and nutritional anemia.

It is clear that some of these diseases are transmitted through such vectors as insects, ticks, mites, or caused by worms and protozoa which are particularly prevalent in the geographical tropics, though I gather that few of them are limited to the tropics by strict factors determining conditions of their biological survival. Certainly, tuberculosis and syphilis still have the widest of spatial incidence, and I am told that typhus flourishes best in climates that are characterized by the cold winter seasons typical of the temperate zones.

Relying upon the authority of Dr. Wilbur A. Sawyer, whose name is well known to this group, I gather that there is a tendency to lump within the definition of "tropical diseases" most of the mass ailments that are exotic to the industrialized areas of the Western World, where the public health programs and advanced medical science have made such spectacular progress toward bringing them under control in the past one hundred years. They are the ailments that are still rife in the lands that economists call underdeveloped and the geographers term tropical rain forest, tropical savanna, and tropical or subtropical steppe or desert areas.

According to this concept, many of the diseases now thought of as typical medical problems in the United States, Canada, Western Europe, Japan, New Zealand and the more developed portions of Australia and South Africa are likely to be classified as tropical diseases at some future date when their incidence has been cut by further advances in our knowledge and procedures and before a comparable degree of control has been established in the underdeveloped areas; just as many, if not most, of the diseases now classified as tropical were once widespread scourges in the temperate zones of the Western World.

If this amateur conception of the general demarcation of your field is not too violently in conflict with your own professional definition, it is apparent that the economist specializing in the problems of underdeveloped areas, the geographer dealing with tropical regions, and the physician, health officer and sanitary engineer specializing in the prevention and cure of tropical diseases are all concerned with problems that fall within essentially common regional boundaries—and that this is strikingly the case if China is excluded as falling outside of the area with which the specialists of Free World countries are in a position to deal.

II

Emphasis on prevention in tropical medicine

There is a corollary principle that seems to be applicable also. If tropical medicine is concerned primarily with control of the mass diseases that pervade the underdeveloped areas of the world, it is fair to note that the medicine and health programs of the more economically advanced countries are in ever-increasing measure concentrated upon the treatment of the degenerative and stress ailments that are masked in the underdeveloped areas by the very prevalence of the mass diseases.

It is conceivable that some of these sicknesses—such as mental ailments and tuberculosis—are directly fostered by the tempo and conditions of urbanization that are incident to the advancement of industrialization. Others, like poliomyelitis, which are popularly thought of as new diseases of the prosperous areas, may in fact be diseases of very ancient lineage and of widespread incidence, but which possibly assume a new virulence when freed of the competition of other infectious diseases. By and large, I take it, the disproportionately high incidence of the degenerative and stress diseases in the areas of relative economic advancement is to be explained partly by better diagnosis but principally because the mass diseases associated with economic poverty mask the incidence of degenerative and stress ailments in the underdeveloped countries. Cancer, heart disease, and diabetes, for example, cannot have comparable clinical importance in the underdeveloped areas where life expectancy averages 30 years, to that which they assume in the advanced economies in which life expectancy at birth averages 63 years.

Tropical medicine, then, would seem to be the medicine of poverty areas, and to call for a preponderant emphasis on preventative measures. By contrast, temperate zone medicine, the medicine of prosperous areas, is more and more placing the greatest portion of its effort upon curative measures. Certainly this is true with respect to its development in North America and Western Europe. This large generalization would seem to be valid with respect to major emphasis regardless of the fact that the need for facilities for the treatment of ailments cannot be ignored in the underdeveloped areas, and still less can preventative measures be neglected in the areas of advanced industrialization.

III

The ounce of prevention vs. the pound of cure

By almost Providential circumstance, the relative cost of the two procedures has at least some correspondence with relative abilities to pay for what is the greatest need in the respective areas. Or, if you prefer, this has been brought about through the historic progress of scientific method applied in response to the manifest need for controlling the scourge diseases in the area in which modern scientific method was developed. It has been said that "cholera was our best sponsor of the health officer."

Economists, in recent years, have been able to assemble data on per capita national incomes which, for all their deficiencies, give some indication of at least the general magnitude of comparative economic levels. I have no intention of burdening you with an elaborate exposition of statistical details. I already have summarized the findings in the statement that the average per capita income in the industrially advanced countries outside the iron curtain—and these countries almost without exception are located in the temperate zones—is more than ten times as large as the average per capita income of the underdeveloped countries almost all of which, as we have seen, are within the geographic definition of the tropics or subtropics.

Obviously, the underdeveloped areas are not able to spare sums for the promotion of health comparable to those that are spent for this purpose in the indus-

trialized nations of North America and Western Europe. Fortunately, there is strong evidence that effective programs for drastically cutting their mass disease incidences, and this is the first need in the underdeveloped regions, can be financed for only a fraction of the cost of combined preventative-curative medical programs such as are maintained in Europe or the United States.

There seems to be sufficient evidence to warrant this statement, though I gather that much work will have to be done before anyone is in a position to make any authoritative estimate of the cost of effective control programs needed to deal with the mass diseases of each underdeveloped country, let alone for all of them combined. Yet we have enough data derived from successful ventures to be reasonably sure of our ground. We have learned that insect-borne diseases like malaria, which is estimated to infect something like 300 million people in the world and to cause some 3 million deaths per year, may be controlled by modern methods at costs varying from 15¢ to 50¢ per capita, and perhaps averaging 25¢. Person-to-person diseases like syphilis and yaws can be made to yield to individual treatment upon a mass basis at a per capita cost of about $2.00. We know that the British comprehensive National Health Service costs something over $23 per capita or about six times as much as the combined national and local preventative services maintained in Great Britain. It has been estimated that reasonably adequate preventative services in the United States are provided at a combined local and federal cost amounting to about $4 per capita of population, while the experience of numerous voluntary medical care insurance programs in this country shows an average per capita cost of $40 per year. There is, then, a variety of evidence to suggest that the control of many of the scourge diseases that undermine the human stamina of great masses of the billion inhabitants of the underdeveloped nations of the Free World could be effected at per capita costs that bear at least something of the same relationship to the overall health expenditures of the industrialized nations as exists between the per capita incomes of the two. Preventative programs appear to cost only about one-tenth as much as curative programs, and the per capita incomes of the underdeveloped areas average about one-tenth of the average in industrialized countries.

I am not unaware of the oversimplification that is inherent in this statement. It is not my intention to gloss over the time or the difficulty of expanding the world's force of physicians sufficiently beyond its present 900,000 to permit such a comprehensive effort, or the still greater task of providing the necessary quota of nurses and other auxiliaries. The magnitude of the task of providing the necessary education prerequisite to the professional training of local personnel for such services is evident. Nor do I wish to underestimate the additional cost of providing the adequate shoes and clothing, housing, water supplies, sewage systems and other appurtenances that are as integral a part of an adequate preventative program against disease as DDT or antibiotics. Further, I am aware that effective control of certain of the scourges, like tuberculosis, which tropical areas share with temperate climes, depends on measures far more time consuming and far more expensive than inhibiting inoculations of BCG, and that the diseases of malnutrition are not likely to be dissipated by a few vitamin pills in areas where

the protein-deficient diet provides only 2,150 calories per day which is the average for the underdeveloped nations as a whole.

Finally, there is a vast gap between the abilities of countries like Great Britain to spend something like 5 per cent of national income on health services of all kinds and of the underdeveloped countries to spend a like proportion of incomes that in many cases are not one-twentieth as large on a per capita basis; and yet, on the doubtful analogy of the $4 per capita estimate of the cost of adequate preventative services in the United States, it would take about 5 per cent of the combined national incomes of all of the underdeveloped nations of the Free World to provide such a per capita sum for preventative medicine expenditures alone.

Despite all of these necessary qualifications, I still feel that the relatively low cost of control measures for the mass diseases is a hopeful phenomenon. It is genuinely fortunate that the immediately pressing medical problem of the underdeveloped areas is that of providing the relatively cheap ounce of prevention rather than the formidably expensive pound of cure. It would seem that the magnitude of an effort sufficiently great to make progressive inroads upon mass disease incidence in the Free World should not be beyond the combined means of the underdeveloped nations' own financing, bilateral assistance, international agency programs and private philanthropy to provide. I hasten to add that I am not thinking in terms of a grandiose $4 billion program. Funds of such a magnitude could not be well employed for a period of many years, even if they could be provided, which they cannot. But, I think that we now have sufficient evidence to be confident that impressive progress along already proven lines can be made at costs that are within the plausible limits of determined cooperative effort on the part of Free World nations.

IV

Tropical medicine progress and the economic interest of the United States

If the above economist's-eye view of the problem of tropical medicine is not as astigmatic as it is sketchy, we may turn to the question of why the United States has a genuine interest in seeing that work in this field is forwarded. Certainly, our direct interest in terms of our own population is limited. In the geographer's classification, only a small portion of our continental territory falls within his definition of the tropics, and our international policy has gone far toward decolonialization of such tropical lands as formerly were administered under our political control. Further, by the definition of tropical medicine that I have tried to formulate, it is concerned chiefly with problems that are less than acute in an area of relatively advanced practice such as ours.

And yet, I think that it can be demonstrated that our stake in the progress of tropical medicine is large and likely to become ever greater in the years ahead. Others on this program have been assigned the tasks of spelling this interest out in its political, strategic and cultural implications, and I take it that one or all of them will touch upon the humanitarian phases of the problem which clearly are deserving of being afforded tremendous weight. I shall confine my remarks to

the strictly economic basis of United States interest, although it is evident that there is the closest linkage between our political, strategic and economic interests, particularly in the world's present uneasy posture that we term a "state of cold war."

The economic dependence of the U. S. on underdeveloped areas

The United States has less than 10% of the Free World's population and about 8% of its land area, but it consumes something like one half of the Free World production of primary materials—48% of its copper and lead, 54% of its iron ore and zinc, 56% of its manganese, 62% of its rubber, and 65% of its petroleum.

Among the countries of the world, we are relatively self-sustaining—in the aggregate, we produce all but about 10% of the raw materials we consume. But in the case of the metals that represent the hard core of our industrial society, we are dependent upon foreign sources for more than 40% of our current supply.

The Paley Commission, in its recent report, estimates that by 1975, assuming that the American economy continues on its historic growth trend, we shall be dependent on imports for no less than 20% of our total material requirements, and in the vital field of metals that 55% will then come from sources outside our territorial boundaries. Unless the economies upon which we depend for such supplies show a tempo of growth sufficiently great to meet the expanding demand of the United States and Western Europe for raw materials, the patterns of economic dynamism that have been basic to our democratic institutions cannot be sustained.

A case scarcely less strong may be built for our stake in maintaining expanding export markets for our specialized production. Export markets in 1952 provided jobs to over 3 million American workers, and accounted for the disposition of about 9% of all the movable goods produced in this country for that year. For many producing groups within the United States the dependence on export outlets is very much larger than the overall average suggests. During recent years export markets took about 38% of United States cotton and wheat production, and our producers of such other items as leaf tobacco, lard, processed milk, machine tools, lubricating oils, tinplate, anthracite coal, and motor trucks and coaches are exceptionally dependent on their abilities to export.

What has this to do with the underdeveloped areas of the Free World? These areas supply the United States with 60% of all its imports and Western Europe nations with perhaps 65% of theirs. On the other side, they provide the market for well over 40% of United States exports, and for almost 75% of Western European exports. The dependence of this country and Western Europe upon the underdeveloped areas for the strategic materials critical to defense is even more dramatic, but that field is the province of another of this afternoon's speakers.

I shall not labor the point further. Quite apart from the political and military considerations of war and cold war, it fairly may be stated that the continued growth in living standards in the United States and Western Europe cannot be maintained unless there is correlative growth in the economies of Free World underdeveloped areas.

The role of tropical medicine in development

The importance of tropical medicine to the task of economic rehabilitation in the underdeveloped areas is another matter that needs no elaboration before this audience. You all are aware of the vicious cycle of disease, low production, insufficient capital to provide for higher production and education and health services, the concomitants of malnutrition, lethargy, and poverty, followed by more disease. No one factor alone will break the dismal cycle, but the effective control of mass diseases is one of the essential links in remedial action.

In comparing the economies of the industrialized and the underdeveloped Free World, the disparities I have referred to in absolute income levels, striking as they are, are less dramatic than the differences in their respective propensities for economic growth. The industrialized West has shown a dynamic improvement in living standards for the masses of its populations as a definite historic trend. This has been particularly marked in the United States where, since 1880, the economy's output has expanded sufficiently rapidly to double the real per capita income of a fast-growing population every forty years. By contrast, the living levels of most of the peoples of the underdeveloped world have appeared to remain constant, and in some cases to have retrogressed.

I believe that it may be stated with confidence, that the high incidences of mass disease have been an important factor in retarding economic progress in the latter areas. Besides its obviously stultifying effect upon human energy, it is evident that mass disease is appallingly wasteful of human resources. In the United States, 90% of the children born live to adulthood, and two thirds live to be 60 years of age. Thus, the span of working usefulness and of production of the average citizen is a long one. In many countries of Southeast Asia and the Middle East only about one half of the children born reach the productive age of 15 and a scant 15% survive at the age of 60. In any accounting of economic productivity, it is clear that important weight has to be given to the ratio between the number of hands able to work and stomachs that require to be fed.

In a true sense it may be said that tropical medicine is the midwife of economic progress in the underdeveloped areas of the world. Where mass diseases are brought under control, productivity tends to increase—through increasing the percentage of adult workers as a proportion of total population, through augmenting their strength and ambition to work, and in many cases by actually making possible the opening of new or the reclaiming of abandoned land previously untenable because of the prevalence of disease. There are many local examples that could be cited to illustrate this thesis in action, but I am sure that all of you can supply them from your direct experience.

The most spectacular case that I know—dramatic because of its large scale—is offered by the record in recent years of Latin America considered as a whole.

General improvements in the health of the area have been accompanied with very evident signs of economic advancement. In the last two decades, the overall Latin-American economy has departed from the dead-center pattern of at best maintaining a given level of income, and has started an impressive march forward. From 1933 through 1952, the real per capita incomes for the 20 Repub-

lies combined has increased at an average rate of 2¼% each year. The magnitude of this achievement is better appreciated when consideration is given to the fact that the Latin-American population is growing at about twice the world average rate, and its physical output has had to increase by more than 2% annually merely to maintain per capita income levels. To achieve the per capita annual gains cited, total output has had to increase by more than 4½% each year.

Earlier in this paper I indicated that there had been a considerable literature upon the question of whether or not a tropical environment was consistent with economic and social progress. I am sure that the coincidence I have mentioned between the geographer's delineation of tropics and the economist's denomination of underdeveloped areas warrants much more searching work than has been done on the effect of temperature, humidity, wind currents and other climatic factors on human physiology and psychology together with further study of how the climate factors may be artificially modified. But in default of confident findings upon human physiology in tropical environments, I believe that the record of Latin America, while too recent to warrant any viewing of the problem through the eyes of Pollyanna, at least should temper the pessimism of those who have been wont to discuss the topic with the voice of Cassandra.

Disease control, economic advancement and population growth

I am afraid that in attempting to outline the basis of an economist's interest in tropical medicine I have been tedious, and I know that I have been overly long. I suppose that I could have said it very quickly and simply in these terms:

An American economist must be interested in the progressive economic improvement of the Free World underdeveloped areas because the continuing dynamism of the economy of the United States is importantly dependent upon their economic growth. He must be interested in tropical medicine, because better control than has yet been achieved of the incidence of mass diseases in the underdeveloped areas is prerequisite to their economic growth. The knowledge required for a continuously better degree of control is at hand, and although the problems of putting such knowledge into practice are formidable, at least the important financial requirement should not be of unsupportable dimension once the importance of the problem to the whole Free World is more clearly recognized.

Alternatively, I might have attempted, with even greater taxing of your patience, to marshall scholarly evidence in support of a variety of conclusions that I have merely stated rather than affirmed.

In either case, I would still hear that insistent voice from the questioner in the back row, saying: "What about the population? If we radically increase the life span through cutting incidence of mass disease, won't we soon have more mouths to feed than our land resources are able to support?"

I wish that I could offer an assured answer. The easy confidence once prevalent that advancing industrialization and urbanization progressively cuts the birth rate has seemingly been brought into serious question by the recent birth trends in the United States and other industrialized societies. We already have evidence of sharply dropping death rates accompanied by apparently rising birth rates in a variety of underdeveloped areas.

The only comforts that I can offer to this persistent questioner in the back row are meager.

First, the problem varies widely in its acuteness among the several underdeveloped nations. Some of them have ample land resources in proportion to population. In others, like India, the problem is very grave.

Second, the acuteness of the problem will be diminished or intensified to the degree that the Free World is able to achieve a relatively unimpeded trading system among expanding economies on the one hand, or moves even further than at present toward the erection of trade barriers of various types.

Third, the possibilities of expanding economic production in most fields are very great—as witness the twenty-year record of Latin America which shows even an increased growth tempo over that cited for the postwar years of 1946–52. Even in the food field, the limits of expandability are far from having been reached. One authoritative agricultural geographer estimates that if cultivation practice on the world's presently cultivated land were brought to the present standard of efficiency now prevailing in Western Europe, it would support about 3 billion people at a reasonable nutritional level. This against the present world population of about 2.4 billion, most of whom are inadequately fed. The same authority, Dr. Dudley Stamp, estimates that if all suitable land in the world were cultivated at the European standard of efficiency, it might support some 10 billion persons. But I gather that this would entail our learning how to use effectively certain tropical lands that we yet do not know how to cultivate with maintenance of fertility.

Fourth, the possibility that there can be major progress in the development and acceptance of effective measures for controlling population growth in areas where there is a major disparity between physical resources and population numbers is certainly of sufficient importance to deserve concentrated attention comparable and correlative to that devoted to preventative medicine.

So the best I can do is to say that we must take some things on faith and that if we were inclined to the position of never handling those problems with which we can cope until we know the answers to all problems our actions might raise, you probably should not have embraced the idealistic profession of medicine, and I certainly should never have entered a craft in which prediction is so tenuously uncertain as it is in economics.

CULTURAL ASPECTS OF TROPICAL MEDICINE[1]

JACQUES M. MAY

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When I received the kind invitation to address this group on the cultural aspects of tropical medicine, I looked in my dictionary to see whether my own not too well defined ideas about culture were in accordance with the official views on the subject. I found that culture meant civilization. Hoping for further enlightenment, I looked up the word civilization, which proved to mean culture. Since the dictionary was no help, I decided to formulate my own ideas about the meaning of these words, and found that if my definition of culture is accepted, the task of discussing with you the cultural aspects of tropical medicine becomes much less formidable than it appeared at first. It is my fond hope that you will share my views on this subject after this discussion is over.

Culture, to my mind, is the sum total of the traits and techniques that man acquires and develops in the process of adapting to the environment, and which reflects the degree of this adaptation. Thus it is forced upon man by the nature of his environment. It is the aim of a highly effective culture to promote and support the survival of the group. Culture is a criterion of man's flexibility and under no circumstances can it be considered as the result of a choice. Naturally, after a number of years have been spent working and living under this culture man is led erroneously to believe that he has selected it.

Civilization, on the other hand, is something different from culture. I would define it as the sum of the traits and beliefs which allow men to live together and thus tend to curb human, primitive instincts or to regulate their expression.

Let us now see the implications of this definition of culture as we consider the problems of tropical medicine.

The best way I can think of to do this is to show you the picture of a woman I met 25 years ago when, as a young French colonial surgeon, I got my first taste of tropical medicine in the country which is now called Viet Nam (Fig. 1). I can truthfully say that more than any other woman I have met in my lifetime Thi-nam has had lasting and profound influence on my thinking and career. I cannot show you a picture of her father, but I could show you a picture of her father's spleen and if I weren't afraid of overstaying my welcome, I might also show you a picture of Thi-nam's uncle's liver, lungs, and other parts of their anatomies.

Not only was I at a loss to find in my young experience or in my well stocked memory of theoretical knowledge any therapeutic answers to such unusual conditions, but I could find no explanation for this illegitimate aspect of pathology. This was not what a well behaved ovarian cyst or a decent French or American spleen would do. As I grew older in the place, I found that other aspects of tropical pathology perhaps less dramatic in outline were just as tragic

[1] Address given before the American Academy of Tropical Medicine on November 13, 1953, Louisville, Kentucky.

FIG. 1. An ovarian cyst, fruit of the delta of the Red River in northern Viet Nam.

in their way of expressing the depth of the sufferings of human tissues. Unusual invasion of organs by worms, deterioration in metabolism shown in a dramatic way by enormous stones in the bladders of children, deep infections creating multilocular liver abscesses not of the amebic type—all caused a very particular pathological picture.

Tropical medicine is not only the study of the diseases that occur predominantly in the tropics—it is also the study of the particular aspect that any disease takes when it occurs under a tropical environment, as well as the study of the little-known variations that occur in human beings in the tropics, whether they are reversible or not, and their relation to the pathological picture. The extent to which the local culture is responsible for these pathological and physiological aspects is what I wanted to find out.

The technical problems, such as removing the ovarian cyst shown above, solved themselves first. It was not very long until I devised appropriate techniques. However, these techniques had to take into consideration a new, at least new to me, human physiology. Certainly it was not possible to inflict on the human beings swarming around me the type of heavy-handed surgical insults that my well-fed and healthy countrymen took in their stride. Certainly I had

to go easy with spinal anesthesia in peoples whose average blood pressure was easily twenty to thirty millimeters below European or American standards. Certainly it would not be wise to inflict the same anesthetic anoxia which did not seem to bother the folks back home on people who at best boasted three million red cells per cubic millimeter. And certainly intestinal surgical techniques would have to take into consideration the swarming world of crawling reptiles of every description that inhabited these intestinal cavities.

Gradually I left more and more of these mechanical accomplishments to my assistants. They seemed rather to enjoy it, up to the time when, in an outburst of sincerity, I told them ex cathedra that I could teach any coolie of average intelligence that swept the floors of the hospital how to become an acceptable surgeon. I added that it would probably take three generations to produce one first rate physician. It has now come to the point where I just cannot understand how a healthy surgeon with normal instincts can fail to become ultimately an epidemiologist, or an ecologist of disease.

If culture is an expression of the people's fight for adaptation to the environment, then what we want to discuss now is the contribution of this fight for adaptation to the production of tropical diseases.

Let us consider the physical environment to which these people have had to adapt. Let us evoke the steps of construction of the milieu and of its settlement by people. I shall of course take as an example the site where I was converted from a surgeon to an epidemiologist.

In Viet Nam as elsewhere the earth, the waters, the winds, and the heat had organized themselves in ways which had resulted in today's relief, hydrography, and climate. I could imagine as the earth was getting colder millions of years ago the crust shriveling to form this northern part of the Annamitic range which continues itself in the very last elevations of the big Himalayas. I could see the torrential rains inflating the springs and forming the mighty Red River, which, fighting its way, century after century, against the tide of the China Sea, had laid the ground for the fertile delta, where the present day people were established. I could imagine what the particular climate had been in the past 10,000 years and the changes it had caused, for we had five months of torrid, steamy summer, four months of lovely, balmy autumn and three months of misty, raw winter. Little by little the present scenery had established itself. In our times it consisted of three concentric terraces presiding over a flat lowland bordered by the sea in much the same way as the balcony, the dress circle, and the orchestra surround a stage. At the top dwelled a few tribes of hardy mountaineers, very sparse, not afraid of fighting big game and living chiefly by hunting and gathering. They had their own diseases, I found out, although I did not see many of them because they very seldom came down to the plain where I was. In the hilly region (the dress circle), there were more villages, although still quite sparse, because only ten per cent of the land could be put to agricultural use. In this middle region one did not find the big game, but rather some deer and a great abundance of *Anopheles minimus*, which throve in the clear running water of the mountain streams.

In the lowlands there was a teeming population, grouped in compact villages

where the density in places reached 1,500 per square mile. In this lowland the Red River was the undoubted imperial master of the country. The river carried fertile alluvial topsoil with which it covered the country-side but also danger in the form of the devastating floods which occurred ever year precisely at the time when the second rice crop was to be harvested. It also shifted its course from one bed to another. Dense population occupied the temporarily abandoned beds, gambling that one, two, or perhaps ten or fifteen harvests of rice could be grown before the neutral river would sweep away crops, houses, and inhabitants. In certain places the effect of the tide made itself felt and there were large pools of salty water, which had a nefarious influence on the crops of the hardy farmers who tried to put the land to good use. Thus for many reasons dams had been built ever since recorded history with various degrees of technological skill until the present day damming program was initiated, engineered, and operated by European experts for the triple purpose of protection, irrigation, and drainage.

The impact of these water problems on the local life was terrific. Without the dams one crop out of two would probably be lost, and widespread starvation would occur. To keep the dams in working order, swarms of laborers had to be recruited, sometimes in a hurry, thus taking them away from the exacting labors of the rice fields and lowering the yield of the crop. It was a matter of computing which way the least would be lost, either making a smaller harvest as safe as possible or taking a chance that the river would not rise to the point of destroying a larger harvest. At one place or another, year after year, populations crowded together in very large numbers, away from their homes, bare legs in the mud, working to the point of exhaustion, plugging, digging, and plugging again to stop the infiltration of water, helped in more recent years by an organized distribution of rations. Once the work was completed, they would return to their villages, sometimes carrying with them the seeds of cholera, collected from other workers who had brought them from their own contaminated hamlets. We shall see later that this labor was not the only reason for mass migrations with their pathological consequences within the delta.

How had these people come to inhabit this exacting region? By studying the way the houses and the villages were distributed one could find convincing evidence that the first invaders came from China in the North, probably during the last century B. C. At first, like all people everywhere, they established themselves in the hills. Men have always been caught between fear and hunger. In the mountains fear was least; there were big distances from one valley to another and the enemy could be seen approaching. But hunger was most, because the everlastingly eroded soil of the slopes was not fertile and only a little of it was arable anyway. So here, as everywhere else, when they felt strong enough men started to make for the plains, where food would be abundant but where some effective protective devices would have to be created, imposing a certain economic burden, creating new habits and new internal problems. This was a very fertile region and under the skilled handling of the Chinese, rice became abundant. There must have been a time of plenty in the now-forgotten history of these settlements. But as always in human affairs, it bred its own destruction. The population increased

in such numbers as to overgrow many times the reasonable density that the land could carry. At first the Chinese conquerors had found there people of Indonesian stock, with a primitive administration. On this element the overwhelmingly powerful Chinese culture grafted itself easily. New agricultural techniques were developed, better administrative habits formed, the rich vocabulary of the Chinese language and the ubiquitous dominant Chinese ideograms were adopted, and last, but not least, Chinese genes were introduced, resulting in a new ethnic type which carried down to our time the still mysterious immunological susceptibilities and protections of age-old central Asian origin. Thus the Vietnamese people were born and, for a certain time, they were mine for study.

Although this mass immigration from the north has been stopped for many centuries because the country is filled to capacity, there still are vast and regular movements of population within the delta. The harvest time is not the same in the north as in the south, in the west as in the east. Armies of field workers concentrate in the regions where the harvest is earliest and gradually move to the places where it occurs latest. You can see them moving on foot on the narrow paths between the rice fields, covered with a waterproof raincoat of tightly sewn banana leaves, carrying their sickles and sometimes a bamboo pole and two baskets, with which they do a little trading on the side.

Once they found themselves in the wide open plains, people had to protect themselves against each other. Thus the villages are compact, easy to defend, if possible surrounded by moats, or thickly fenced in by a bamboo hedge, in the beauty of which the villagers take a deep pride. Severe punishment is meted out to those who pick a bamboo leaf, or in any way injure the hedge, yet children make good use of holes and passages known only to themselves to get in and out without using the communal pathway and passing through the monumental door. In most cases these doors are thick and solid. They are closed at night and nothing is more difficult than to enter a Vietnamese village after curfew if you are not familiar with the locality.

The most favored inhabitants have their houses near the rim of the village and have a sort of jetty which juts out onto the pond. This is convenient. It is a sort of bathroom attached to the house, where the family can take a shower by ladling out the chocolate colored water. It also provides a kitchen sink to wash the rice, the dishes, and the laundry. It is also convenient for the raising of fish and water cress used to feed the pigs, and in the lean years after the pigs have been eaten, to feed the men. However, the water itself is not drunk, except on rare occasions. The Vietnamese of the delta likes to drink rain water which he collects in cisterns and sometimes in jars and bottles, which he sells as medicine after it has been held many years.

If the climate, land forms, and customs govern the layout of the villages, they also govern the layout of the houses. The material of which their dwellings are built is, of course, the material that is available—its architectural potentialities govern the type of house. Lumber is scarce in the delta but abundant in the mountains; mud and straw are common in the delta but scarce in the mountains. We shall have to remember this when we try to understand the malaria pattern. In

most dwellings there is a central yard and in the back the house proper and the altar of the ancestors. On each side of the yard, in separate buildings, are the storeroom where the rice is kept, and the pigsty. These pigsties are sometimes closed by thick boards which come from coffins that have been disinterred after a reasonable amount of time to collect the bones which are then put in sacred shrines. These thick boards are reputed to give the pigs rapid growth and good health. Occasionally they are also used to protect the room where sick children are resting, as it is surmised that such horrible sights will chase away the evil spirit that has invaded the body of the child. The house itself is covered by a roof, rarely of tiles, but usually of rice straw thatch. The floor is beaten earth and the walls are dried mud from the rice field, filling in the spaces of the woodwork.

Now that we have seen where these people live, let us see what they eat. Rice, of course, and polished rice at that. Of course production of enough rice to support the population is the problem. I will not discuss with you here the fantastic edifice of mortgages and debts which rises above the fraction of an acre of land on which the family life is built. Nor shall I describe the land tenure laws and customs that have resulted in the reduction of the size of property through the years to insignificant proportions. Suffice it to say that both factors have a definite significance in terms of scarcity and starvation, hence a direct influence on the pathological picture of the country.

The problem of fertilizing these fields is vital. The farmers of the delta are well aware of the value of human fertilizer. In the villages human night soil is carefully collected, and in some places where there is a surplus, a brisk trade is initiated with villages of lower yield. In the evenings after their day's work is finished women gather the stuff and start on their endless trips balancing it on their shoulders in baskets at both ends of their bamboo poles. Urine is also collected and used for the most promising cultures. Animal fertilizers from pigs and buffaloes is also used as well as end products of fish which have been allowed to rot to produce a local spice called *nuoc mam*.

During two thirds of the year the delta is practically under water. Hence, every farmer is a fisherman. He sends his children after snails, crayfish, and crabs as soon as they can walk, and these are a welcome addition to the daily diet. In these private ponds that surround the villages, fish is developed as a local industry. A few specialists get the best species (those which do not feed on other fish) from the banks of the Red River and bring them back to these ponds for breeding. They are skilled in the diagnosis of the best places where the fish can be caught and they have developed a number of tricks. They watch the clouds, which indicate the time and place where fishing is going to be most rewarding. They watch the twigs floating on the river, or the color of the foam, which gives a clue as to the origin of this particular mass of water and hence of the fish that can be found in it. They send their buffaloes in the narrow streams to shake up the mud in the middle, forcing the fish to swim near the banks.

In certain areas of the delta the water people concentrate in floating villages, making a living by fishing or by water transportation. They pay dues to the nearest village for the privilege of burying their dead and sometimes of having a

place of worship and a town hall. But in most of the 100-odd such villages these civic and religious activities occur in a floating building.

All this is chiefly fresh water fishing. The offshore waters are too shallow, the sand banks extend too far into the China Sea to allow for the development of sea fisheries, and out of a population of several millions only very few fishermen try the salt water for its product. This explains why beside rice and yams, it is chiefly crayfish, snails, and fresh-water fish that compose the menu of the people. Of course, there are lean years and fat years, but in most cases the average consumption of food does not exceed 1,800 calories at best and is low in animal protein.

Thus, the people who live in the delta of the Red River survive. They have acquired a culture which has so far allowed them to adapt to the environment in which their ancestors settled. If this environment has fostered a certain type of life upon human beings it has done the same to animals and plants. But this aspect of the factors that contribute to a pathological picture, however important, is outside the scope of today's discussion. We can only say that situations have been created in this fight for adaptation which have a direct bearing for better or for worse upon the disease pattern, frequently by promoting or destroying the effectiveness of a vector or of an intermediate host.

It can be summed up thus: from the waters the people get their food, also their cholera, their dysenteries, their typhoid fevers, their malaria; from the earth they get their hookworm; from the crowded villages they get their tuberculosis and their yaws; from the type of housing they have been forced to adopt they get their plague and typhus; and from the food which earth, temperature, and rain produce, their protein deficiencies, their beri beri.

Some of the details in this chain of correlations between culture and disease are particularly worth noting: a combination of natural and man-made factors determines the way the houses are built. In the delta, where mud and straw are not conducive to sky-scraping architecture, the houses are on the ground. The pigsties and the kitchen are at some distance from the dwelling. It is fortunate that the species of mosquitoes found in the delta are not effective vectors, because if they were there might not have been any large settlement there. In the hills, on the other hand, the houses are of lumber and built on high piles. The pigsties are under the house and the cooking is done in the living room, thus malaria vectors are given a chance to feed on animals rather than on man, and in any case the fumes of cooking chase them away.

Although no large settlement has ever prospered in the hills local tribes manage to survive. But when the man of the delta moves into the hills, bringing with him his own type of culture, he falls an easy prey to the fierce vectors which he is not equipped to avoid. From the conditions I have mentioned previously, it comes as no surprise to you that we find a correlation between the distribution of hookworm incidence and that of night soil utilization and houses built on beaten earth. We have noted the compactness of the villages, the nearness of the food storage places to the houses, the presence of straw thatched roofs, and you have guessed, of course, that this provides an ideal environment for plague-bearing rats and for a great degree of commensality between rats and men. Last but not

least, when I told you of the rice diet, the connotation of diseases of rice, such as beri beri, was implicit, especially when I mentioned that polished rice was preferred. In this respect it is interesting to note that an increase in the rate of beri beri occurred when village mortar and pestle polishing of rice was replaced in certain areas by mechanical instruments which did a bigger and a better job of causing beri beri. And when I noted that there was little animal protein in the diet, you were not surprised to hear about the huge stones which grew in the bladders of infants.

We have seen the importance of the ponds and moats around the villages. And we have described the infiltrations of waters through the dams imposed upon the population by the morphology of the region. The pattern of water pollution both above and below the surface is governed by this factor, which also combines with the various migrations within the delta to create the local geography of cholera. We have mentioned the many uses of these ponds, the growth of the water cress on their surface and the importance of fresh-water fishing in the culture of the delta. This, of course, results in the delta of the Red River being one of the most fertile in helminthic diseases related to water-borne animals. It is one of the few foci of *Clonorchis sinensis* to be found outside Japan or China. It is one of the richest foci of *Paragonimus westermani*. The big intestinal fluke *Fasciolopsis buski* is common.

Naturally when the physician comes into a new tropical land all that he sees are individuals like Thi-nam and her brothers and sisters, and it is up to him from this starting point to grope in the darkness of uncertainty and ignorance to find the innumerable cultural factors which have brought about the conditions he is called upon to cure. Although the chain of events conducive to a given picture is inexorably established, no state of equilibrium is ever reached. I suppose this occurs only in heaven.

I have attempted to describe a given environment and to show how the people's fight for adaptation resulted in a certain disease pattern. I have found this to be true not only with the Red River but everywhere else I have been.

Many years later, in Central Africa, the picture of disease was entirely different. For some mysterious reason, there were no large ovarian cysts, no large bladder stones in infants, and no liver abscesses, but enormous scrotums, sweeping the floor; strange tumors in the rectum; black water fever, this latter, of which I had seen but very few cases in Southeast Asia, occurring chiefly in transplanted white men. There was no cholera, but sleeping sickness; practically no dengue, but yellow fever. It had been the reverse in Indochina. There was no *Clonorchis sinensis* but plenty of schistosomiasis. I could go on for a long time. In Central Africa tuberculosis was doing a quick job of men, whereas in Southeast Asia I had seen people going to their work with cavities as big as my fist and apparently none the worse for it. Still later, in the American tropics, the general pathological face of the region changed once more—no swollen scrotum, but plenty of lymph in the urine; malaria, but no gigantic spleen; no liver abscesses; no cholera, but a local form of trypanosomiasis; different spirochetosis, such as I had never seen

before; practically no plague, but a concentration of leprosy greater than in my previous experiences.

It is possible to find a key to these various geographical aspects of pathology in a careful study of the local culture. An analysis of the environmental factors, followed by a study of the cultural traits these have fostered reveals the epidemiological mechanism which brings about the pathological facts that we observe.

In every country where people live for any length of time and where physicians are called upon to take care of their ills, there is water, earth, wind, and temperature. The arrangement of these various elements varies infinitely for reasons we do not fully understand. But we can study these arrangements and the way people create techniques and guiding principles to adapt to them. These are the cultural factors that shape the pathological picture in the various geographical areas. A good knowledge of these cultural factors, of this ecology of disease, is in my mind the most important lead to our ultimate aim: control.

POLITICAL IMPLICATIONS OF GLOBAL TROPICAL MEDICINE

FRANK P. CORRIGAN[1]

A symposium of this kind is useful in bringing to public attention the importance of tropical medicine and the ravages of tropical diseases as they occur in much of the globe which lies outside of the limited area comprised between those two imaginary lines—the Tropic of Capricorn and the Tropic of Cancer, the geographical designation of the tropics. There is no need to tell a gathering of this kind, but the general public needs to be educated to the fact that tropical diseases (so called) are not limited to the tropics. Only this morning I was discussing the epidemic of amebic dysentery which many surgeons, Fellows of the American College of Surgeons, picked up at the Clinical Congress of that organization in Chicago in 1933. Other striking examples like the historic yellow fever epidemics in Philadelphia and New York have been almost forgotten.

Political factors and political developments play a great part in the desolate picture presented by high percentages of preventable afflictions over large areas of the globe's surface. This political influence has both negative and positive aspects. You are all familiar with local political obstacles that crop up everywhere —scrimpy budgets for health as against lush appropriations for military expenditures, opposition to public acceptance or public avowance of a local epidemic, public knowledge of which might have unfavorable political repercussions. Refusal to acknowledge undesirable facts may allow the evil to become so widespread that it becomes of necessity common knowledge, while honest acceptance of the first outbreaks and unhampered efforts toward control might have isolated the focus of disease and prevented a greater calamity. Everyone who has worked in public health can recall experiences of this kind. This negative political obstruction is not confined to any country or any geographic region. I have known personally many of the courageous men who have stood upon their own firm feet and bearded political lions in their dens.

I recall an incident in the life of General Gorgas, then but a Major in rank, who was called to account by his very able superior officer the Engineer in charge of the construction of the Panama Canal. The interview went something like this: "Gorgas, I have been looking over the cost accountant's figures and they show that every damn mosquito you have killed is costing us $5.00" Gorgas, in his mild manner, replied: "I wouldn't think of disputing your figures, but wouldn't it be too bad if one of those $5.00 mosquitoes that we had failed to kill should bite you in your sleep and deprive us of your valuable services?" I have a picture in my mind of Hanson striding angrily into the sacred precinct of a presidential palace, dressed in his field equipment with engineer's boots outside his trousers legs (hardly a formal garb for a presidential audience), brushing aside well intentioned defenders of the President's privacy demanding and getting the authority he needed to go up to Paita and combat a yellow fever

[1] President, The Latin American Foundation; Representative for International Affairs, American College of Surgeons; Observer, the United Nations, N. Y., and WHO, Geneva.

outbreak that was *politically undesirable*. He, himself, contracted yellow fever on that expedition. The monograph that he wrote of his own personal experience with the dread disease that nearly killed him is, to my mind, one of the classical papers of medical literature.

I witnessed at close hand over a period of years the skillful medical diplomacy of Dr. Molloy in Central America and I am proud of the record left by these men and others like them who were my friends. One could go on reminiscing at length about these local political aspects of tropical medicine. Like conditions exist and similar problems arise everywhere. Triumph over these obstructive political factors has brought about improved conditions in many places. These bright spots represent the fragments of an incomplete mosaic to which additions are being gradually made.

Progress in world health work which was going on apace was disturbed by that calamity which is the most negative force of all—WAR. In war health measures and human life itself are subordinate to other considerations. This has often been a grave mistake which has resulted in military disaster. There are many historic examples: Napoleon's grand army, victoriously penetrating Russia to its heart at Moscow, was struck down by typhus. General LeClerc, brother-in-law of Napoleon, started out to occupy New Orleans with a veteran force of 50,000 men. En route he had the detail putting down a small focus of rebellion against France in the Island Republic of Haiti. His great army was completely destroyed and he himself lost his life. The Haitian heroism received considerable help from the native yellow fever and malaria-carrying mosquitoes.

The defeat of this great French Army, which was headed for New Orleans, had a tremendous effect upon the development of our own West, since, as a direct result, came Jefferson's negotiations with Napoleon and the Louisiana Purchase which gave us thirteen additional States and control over the great Missouri and Mississippi river valley. More recently, during the Spanish-American War, our soldiers suffered far greater casualties from typhoid than from Spanish bullets. The Japanese learned a great lesson from our failure in sanitation and learned it well. The political effect of their learning this lesson was terrific and had much to do with what later happened in China and with later Japanese military development up to their successful attack on us at Pearl Harbor. Most recently in China the epidemic losses amongst the Communist forces were so great that the germ warfare lie had to be introduced as a measure of defense of the officials concerned. That is a most glaring instance of the political psychology mentioned in the first part of this paper. The officials went from mere suppression of bad news to the point of ascribing the outbreak of an epidemic which they could not control to the work of a diabolical enemy. The political pressure upon them to take this rash step must have been enormous. The forum of the United Nations brought their great lie out into the open. War promotes disease and spreads it to areas which would normally be free from certain epidemics. The coordination of the work of dispersed and regional movements for better public health was progressing well after the first World War, during the peace years which are always the years of opportunity. This progress was disorganized by the holocaust

of the second World War. Many of the lessons taught by history were forgotten or ignored. Thousands were sacrificed unnecessarily by epidemic disease, as they had been in the past. The campaigns in the Pacific and Asia furnish many examples.

With the War's end the weary struggle of mankind for better conditions began anew. The logical result of human craving for the blessings of peace following the course of war was a new attempt at formation of a world peace organization. Springing from this universal desire came the organization of the United Nations in San Francisco in 1945. It was to be stronger and better than the defunct League of Nations. Its purpose was stated in the first line of its charter, which reads: "We the peoples of the United Nations determined to save succeeding generations from the scourge of war. . . ." I like to compare the United Nations to a giant tree. Its roots spread out into the soil of all the peoples of the world, organized and unorganized. From these sources come its nourishment and strength. There are meeting at this moment in New York representatives of more than one hundred affiliated nongovernmental organizations which are contributing their ideas and their efforts to its success. Let the trunk of the tree represent the political unity of the world, and the branches the specialized agencies which bring forth the fruit, and by these fruits they shall be known.

The specialized agency with which we are most concerned is the World Health Organization. This organization has more members than the parent body of the U.N. because it pursues a more liberal membership policy. It came into official being actually only in 1948, when the first General Assembly was held in Geneva. I had the privilege of being a member of the U. S. Delegation at that inaugural meeting. The impact of this new coordinating force in world health was felt immediately for under its auspices came the first real *world* mobilization against the cholera epidemic in Egypt in that same year. It has become a central agency for such organizations as the Children's Fund, the Food and Agricultural Organization, the Technical Assistance Program, in all of their work which influences public health. Through these combined efforts there is hope that the mosaic referred to above will make rapid progress towards completion and the picture that it formed will be one of well integrated global planning for the health and well being of the peoples of the world. No other accomplishment can do so much for the cause of peace. Interference with this development by a third world war would be an immeasurable catastrophe which might destroy the civilization that we have known.

UNFINISHED BUSINESS IN TROPICAL MEDICINE[1]

HENRY EDMUND MELENEY

The American Academy of Tropical Medicine was founded on February 6, 1934, at a two-day conference in Washington, D. C., attended by 41 representatives of 35 medical institutions and other agencies interested in tropical medicine. The meeting was held under the auspices of the Division of Medical Sciences of the National Research Council and was made possible by a grant from the American Leprosy Foundation, whose President was Mr. Perry Burgess. The moving spirit in the conception and organization of the Academy was Earl Baldwin McKinley, then, at 39 years of age, Dean of the School of Medicine of George Washington University.

McKinley was a man of both vision and action, who had already had a breadth of experience rarely matched by a man of his years. Born in Emporia, Kansas, he received his M.D. degree from the University of Michigan in 1922, meanwhile teaching bacteriology and biochemistry. Without taking an internship he held positions during the next six years successively at Baylor, Brussels, Columbia, and Manila, and was then called again to Columbia with the rank of Professor of Bacteriology, and was made director of its affiliate, the School of Tropical Medicine of the University of Puerto Rico. There he remained for three years, when he was called to George Washington University in 1931 as Dean of the School of Medicine (Soule, 1939).

In 1929 at the height of postwar prosperity, some wealthy philanthropist, apparently fired by McKinley's enthusiasm, contemplated endowing the study of tropical medicine in the United States with 40 million dollars, but the financial crash nipped that dream in the bud, and McKinley decided that if financial support were to be obtained it would require presentation of facts as to the importance of disease in the tropics. He therefore determined to make a survey of tropical and related diseases throughout the world. He got the National Research Council to appoint an Advisory Committee and obtained a grant from the American Leprosy Foundation to defray expenses.

At the meeting of the American Society of Tropical Medicine in Richmond in November 1933, McKinley read a paper on the "Development of Tropical Medicine in the United States," and in it mentioned his survey which was in progress. At this time the Society was starting a period of renewed activity. Membership was increasing rapidly, a new Constitution and By-laws were adopted, and a committee was appointed to establish a Society Medal, now the Walter Reed Medal.

It was in the atmosphere of this increased interest in tropical medicine and McKinley's enthusiasm, that the American Academy of Tropical Medicine was founded in February 1934. I remember vividly the optimism which pervaded that

[1] Presidential Address. Read at the twentieth annual meeting of the American Academy of Tropical Medicine, Louisville, Kentucky, November 13, 1953.

organizing conference where most of the leaders in tropical medicine in the United States met and saw the prospect of great advances and more adequate financial support for their field of interest. A Constitution and By-laws for the Academy were drawn up, stating its purposes to be:

(1) "To further the extension of knowledge for the prevention of human and animal diseases of warm climates;"

(2) "To provide a current survey of work in progress in tropical medicine;"

(3) "To coordinate American work in tropical medicine;"

(4) "To function as a central source of information;"

(5) "To cooperate with other agencies interested in maintaining and obtaining support for tropical medicine;"

(6) "To receive funds and administer them through grants-in-aid and in support of definite projects related to the purposes and aims of the Academy."

Theobald Smith was elected President and McKinley Secretary. The officers and councillors were empowered to elect fifty charter members, and the roster was announced three months later. At the final dinner tendered to the organizing group President Cloyd H. Marvin of George Washington University announced that the University would establish a gold medal to be awarded periodically by the Academy. Theobald Smith died on December 10 of that year, and the medal, when established in 1936, was named after him. McKinley also dedicated to Theobald Smith his survey entitled "A Geography of Disease" which appeared in September 1935. It was a volume of 495 pages published as a supplement to the American Journal of Tropical Medicine.

McKinley's desire to obtain substantial funds to implement the objectives of the Academy led to the passage of a Resolution at the organizing conference requesting the Leonard Wood Memorial (the American Leprosy Foundation) to consider the formation of a Foundation of Tropical Medicine. In July, 1934, Mr. Burgess wrote a long letter to the Council of the Academy saying that the Directors of the Leonard Wood Memorial had decided that expansion of the activities of the Memorial to the broad field of tropical diseases could not be undertaken, and that the Board could not assume the responsibility for the creation of a separate foundation. Mr. Burgess also suggested that if the functions of the Academy did not include public solicitation of funds it should call a conference of official executive representatives from all institutions in the United States doing any work in tropical medicine to consider whether a Foundation of Tropical Medicine was needed, what its character, functions and relation to those medical institutions should be, how much money would be needed for the next five years, and whether such a Foundation would fill a real gap without overlapping, and would strengthen the programs of interested institutions. Mr. Burgess recommended that if such a conference considered a Foundation important and desirable, a group of outstanding laymen be invited to become members of the Board of Directors. He recommended strongly that no medical man be a member of the Board. Later it was decided that, because of the difficulty and expense of calling another conference, McKinley should prepare a brochure covering the entire project, and send it to the heads of institutions having an interest in tropical

medicine. This he did with the approval of the Council of the Academy late in 1934 (McKinley, 1934). He requested that each institution, after study and consultation should state whether it was interested in such a movement and whether it would favor and support the development of a Foundation of Tropical Medicine. Replies were requested before April 16, 1935, when the first annual meeting of the Academy was to be held in New York.

At that meeting, Vice-President Craig presided and read a eulogy to Theobald Smith who had died the previous December (Craig, 1935). I have not seen the minutes of the meeting, but the general sentiment of the replies received from the institutions must have been favorable, for at the next meeting of the Academy, held in conjunction with the meeting of the Society of Tropical Medicine in St. Louis in November 1935, announcement was made of the formation of the American Foundation for Tropical Medicine. The announcement, which is included in the report of the Secretary of the Society, Alfred C. Reed, states that the organization of this Foundation "is the result of the combined action of the Council of the American Society of Tropical Medicine and the American Academy of Tropical Medicine" (Reed, 1936). Its organization was consummated following a symposium on "Economic and Social Features of Tropical Medicine in the United States," arranged by the Councils of the Society and Academy. The speakers were three laymen interested in tropical medicine, Mr. E. B. DeGolia, a wealthy hotel owner of San Francisco, Mr. Perry Burgess, and Mr. Lyman Pierce, a professional money raiser.

The first directors of the Foundation were predominantly university presidents and other laymen, and McKinley was named Executive Director, while Ernest Carroll Faust succeeded him as Secretary of the Academy and retained that position for 13 years. The Academy, being thus relieved of fund-raising responsibility, took no further action toward implementing its own program, but awaited the acquisition of funds by the Foundation in order to carry out the purposes expressed in its Constitution. Little progress in fund raising was made in 1936, and in 1937 McKinley had a sabbatical leave which he spent in the Philippines. Then on July 28, 1938, while on another trip to Manila, the airplane "Hawaii Clipper" on which he was a passenger disappeared off the coast of Mindanao, and after fruitless search, its passengers and crew were declared lost at sea. Thus ended a brilliant career and the immediate prospects of a vigorous financial campaign.

At the annual meeting of the Academy in November, 1938, Thomas T. Mackie was designated the official representative of the Academy to the Foundation. This made him in effect the Executive Director in McKinley's place, and when the Foundation was reincorporated in the State of New York in 1940, Mackie became its President, and held that position until he recently graduated to be Chairman of the Board of Directors.

While Mackie was in military service during World War II, Jean A. Curran assumed the directorship of the Foundation and designated his assistant, Mr. Alfred R. Crawford as its Secretary. Because of the great importance of tropical medicine in that war, the Academy, at its meeting in Cincinnati on November

17, 1943, authorized its President "to appoint a committee to clarify the relations of the Academy to the Foundation program, and to make specific recommendations in order to activate the provisions of the constitution of the Academy with respect to education and research in tropical medicine." Wilbur A. Sawyer was made chairman of this committee. Its report was approved by the Council of the Academy and was submitted to the Foundation in February, 1944. In the report the division of functions of the two organizations was described. The Foundation had the responsibility for negotiating and approving projects and appropriating funds for their support, and could maintain and finance the necessary staff. The Academy, said the report, "can accelerate progress in the field of tropical medicine by making authoritative pronouncements as to the needs in that field, by recommending general programs to the Foundation when requested, by answering inquiries as to the advisability of specific projects of the Foundation in their general features, and by giving moral support to the movement to improve teaching and research." The report also stated that "it would seem unwise for the Academy to operate even an information bureau, since the most reliable advice . . . could be made available by reference to the institutions and individuals most qualified to reply." The report then recommended that the Foundation assist or create three strong schools or departments of tropical medicine, one in the South, one on the Atlantic Seaboard and one on the Pacific Coast; that it make available grants-in-aid and fellowships; that it assist medical schools to improve their teaching; that it subsidize the American Journal of Tropical Medicine and the Journal of Parasitology; and that it support exchange of professors between foreign and American institutions teaching tropical medicine.

I have referred to this report at some length because it expressed the considered opinion of a strong committee as to the functions of the Academy, giving it an advisory rather than an operating role in promoting tropical medicine. The program and recommendations of the Academy, as expressed in the report, were "unanimously endorsed by the Academy and approved by the American Foundation for Tropical Medicine," and were published in Science, April 21, 1944 (Sawyer and Faust, 1944).

It is impossible and inappropriate at this time to review in detail the accomplishments and difficulties of the American Foundation for Tropical Medicine. Suffice it to say that through the years, under the presidency of Dr. Mackie, it has raised several hundred thousand dollars, has provided fellowships to Latin American physicians to study at Tulane, has provided grants-in-aid to a few medical schools, has subsidized the American Journal of Tropical Medicine and the Journal of Parasitology, gave assistance to the Fourth International Congresses of Tropical Medicine and Malaria, and has supervised the scientific and technical exhibits at meetings of the Society. It has established the Liberian Institute for research in tropical medicine through a gift from the Firestone interests, and this year appointed Dr. Max Miller as its first director. But its administrative expenses have always been greatly out of proportion to its income, and it has not been able to attract the large sums necessary to carry out the program envisioned by the founders of the Academy. It remains to be seen

whether, with its reorganization under the presidency of Mr. John Abbink, it can fulfill its intended functions.

Probably the greatest concerted effort of the Academy was its initiation of the movement to hold the Fourth International Congresses of Tropical Medicine and Malaria in Washington, D. C., and the participation of many of its members in the planning and conduct of the Congresses. This activity was suggested by Mark F. Boyd when he was President of the Academy in 1945. Louis L. Williams obtained the official sponsorship of the Department of State, and in 1947 Wilbur A. Sawyer became Executive Secretary of the Organizing Committee. Through his administrative skill and the cooperation of many agencies and individuals, the Congresses, held in May 1948, were of exceptional value and interest to the delegations from all parts of the world (Faust, 1949).

The officers and Council of the Academy have occasionally expressed interest in national legislation affecting world health. They communicated with members of Congress in support of the International Information and Cultural Affairs program of the Department of State, and in urging membership of the United States in the World Health Organization.

In 1950 George Washington University notified the Academy that it could no longer continue to sponsor the Theobald Smith Medal, which had been awarded in alternate years since 1937. Through the generosity of two members of the Academy the medal became the property of the Academy and was awarded in 1951 and again this year. It is now financed by the dues of the Academy, which were increased from two to three dollars for that purpose.

I have given this dry and detailed account of the establishment of the Academy and the Foundation in order to bring into perspective the question of the future role of the Academy. It was established as a working organization, not as a merely honorary one. But when it was relieved of its fund raising functions it became primarily honorary in character. In 1940 its membership limit was increased to seventy-five in order to provide recognition to younger men who had made important contributions to tropical medicine. This, however, did not increase its activity, and has still left considerable achievement unrecognized. This year it is voting on an amendment to increase its membership to 100 in the hope that this will bring in younger minds to stimulate and guide it into greater usefulness.

Last year the Academy appointed a committee to recommend what its future should be, and the Society appointed a liaison committee to cooperate with the Academy's committee in making recommendations. These two committees held a joint meeting last Wednesday evening, and their report will be presented to the Academy and the Society to-night and to-morrow.

There is obviously much unfinished business in tropical medicine. With the decrease in the ravages of plague, cholera, yellow fever and malaria, other more difficult problems such as schistosomiasis, trachoma, nutrition, animal diseases and general sanitation assume relatively greater importance; and hitherto unrecognized diseases and health problems appear. Tropical medicine in the United States requires continuous stimulation in research, teaching, fellowships for study

abroad, and guidance to the federal government and commercial agencies on their assistance to and development of tropical regions. I believe that the Academy or the Society can be a potent force in this stimulation. One facility which would aid it materially is a headquarters in Washington which has been suggested by Dr. Fred L. Soper. An office, provided by some interested agency such as the Pan-American Sanitary Bureau, and an executive secretary, made possible by a subsidy from the Foundation for Tropical Medicine, could be a focus from which promotional activities could be conducted and from which a program of scientific meetings could be arranged, with emphasis on addresses by authorities from foreign countries, practically all of whom visit Washington. Among its promotional activities could be the encouragement of fellowships for teachers and students of tropical medicine to travel and study in the tropics. It might also act as the Washington office of the Foundation for Tropical Medicine. Finally it might act as the executive office of the American Society of Tropical Medicine and Hygiene, with a paid secretary-treasurer to handle the increasing business of that organization, and be responsible for the publication of Tropical Medicine News.

We should not complain if tropical medicine in this country is neglected by governmental agencies, philanthropic foundations, educational institutions and business concerns. "The fault, dear Brutus, is not in our stars but in ourselves, that we are underlings." If we need better facilities for accomplishing our purposes we should create them, for that is the way all progress is attained.

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INTESTINAL PROTOZOA, HELMINTHS AND BACTERIA IN TAHITI, FRENCH OCEANIA[1]

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This survey reports the results of examining stool specimens for protozoa, helminth eggs and Gram-negative, non-lactose-fermenting bacteria. As the study progressed it was possible to assemble information concerning the comparative efficiency of the methods employed in examining for protozoa. These are discussed in relation to other reports. Also, complement fixation tests were made on the serums of twenty-five individuals known to be positive for *Entamoeba histolytica*.

METHODS

Individuals selected for this survey fall into three groups:

a) Three hundred presumably healthy individuals from schools and homes in the districts of Papara and Mataiea.

b) Two hundred individuals from the French Colonial Hospital in Papeete who did not exhibit gastro-intestinal ailments.

c) Sixty clinic and hospital patients with acute gastro-intestinal symptoms. See Thooris and Kessel (1953).

Fifty persons were examined in each age group, as indicated in Table 1.

Three stool specimens were collected from each person, as nearly as possible on three consecutive days. All stools were examined in the laboratory by the following procedures:

a) Direct preliminary film in saline and iodine (Kessel, 1944). The complete area of a 22 mm. cover glass film was examined, using a 4 mm. objective and a 5× ocular.

b) Permanent iron-hematoxylin film (Kessel, 1944). The complete area of a 22 mm. cover glass film was examined, using oil immersion objective and a 5× ocular.

c) Zinc sulfate flotation, after the method of Faust (Faust *et al.*, 1939), with examination of the complete area of a 22 mm. cover glass with 8 mm. objective and 5× ocular.

d) Culture on S. S. medium for *Shigella*, *Salmonella* and other Gram-negative non-lactose-fermenting rods.

RESULTS AND DISCUSSION

1. *Organisms encountered*

a) *Animal parasites.* Table 1 lists the number of individuals positive for each parasite in each age group of fifty persons and an additional 10 individuals of

[1] This study was made possible by special contributions from Cornelius Crane to the Pacific Tropic Diseases Project, School of Medicine, University of California, Los Angeles.

TABLE 1

Intestinal parasites

Total number of persons: 560

PARASITES	NUMBER POSITIVE IN EACH AGE GROUP												TOTAL +	%+
Age Groups	0–4	5–9	10–14	15–19	20–24	25–29	30–34	35–39	40–44	45–49	50+	Unknown		
E. histolytica	3	7	11	14	13	13	13	7	17	13	12	2	125	22.3
E. coli	9	16	15	15	14	14	16	8	10	15	11	1	144	25.7
E. nana	7	17	18	25	12	22	22	15	24	19	11	3	195	34.8
Iodamoeba	2	1	4	7	5	7	5	3	1	2	5	1	43	7.7
Enteromonas	10	15	8	9	5	9	10	8	13	10	11	2	110	19.6
Giardia	10	9	6	4	6	7	5	3	2	3	2	—	57	10.0
Chilomastix	3	1	2	4	3	1	3	1	2	3	4	—	27	4.8
Trichomonas	2	0	4	4	2	5	1	0	1	1	7	—	27	4.8
Dientamoeba	4	6	3	8	8	1	11	10	6	2	2	—	61	11.0
Balantidium	0	0	1				1						2	0.4
Isospora				1			1						2	0.4
Trichuris	21	37	30	24	25	18	25	17	18	15	16	1	247	44.0
Hookworm	9	30	30	23	19	10	12	17	18	27	16	4	215	38.0
Ascaris	12	17	10	11	7	2	5	3	2	0	2	1	72	12.9
Enterobius	0	5	6	0	2	0	0	0	0	1	1	0	15	2.7
Strongyloides	0	1	1	0	1	0	4						7	1.3
Hymenolepis						1							1	0.2
Opisthorchis											1		1	0.2
Negative	16	4	1	6	5	3	5	12	8	8	12	3	83	14.8

unknown age. The percentage positive in each age group therefore is twice the number recorded.

Of special interest is the fact that 22.3 per cent were positive for *E. histolytica*. If one deducts the 60 clinic and hospital patients who exhibited acute gastrointestinal symptoms, it is found that 19.2 per cent of the remaining 500 are positive for *E. histolytica*. Eyles *et al.* (1953) in a recent survey estimate the actual prevalence rates of the area in which they worked to be "half again as high as the observed rates."

Giardia occurred in 10 per cent of the persons examined. As is usual in most surveys, *Giardia* was found to be more prevalent in the younger age groups, occurring in 17 per cent of those under 14 years of age. It will be noted that *Balantidium coli* and *Isospora* sp. were each encountered twice.

Trichuris is the most prevalent helminth found in Tahiti, 44 per cent of the people in this survey being positive.

Hookworm is second in prevalence, 38 per cent of the individuals being positive. Hookworm egg counts for the most part were low, usually under 2,000 per gram of feces, and little hookworm disease is encountered. During the survey, only 5 cases were found to have egg counts above 2,000 per gram of feces.

Only 12.9 per cent of the people examined in this survey harbored *Ascaris*. This is in marked contrast to the high percentage of *Ascaris* reported in many

surveys in tropical areas. *Enterobius* was found in 2.7 per cent of the stools. *Strongyloides* was found seven times, *Hymenolepis* and *Opisthorchis* each once, the last being found in a Chinese, born in Polynesia, who probably acquired the infection from eating imported dried fish.

b) *Enteric bacteria.* Table 2 lists the Gram-negative non-lactose-fermenting rods isolated. Thirty-five individuals or 6.2 per cent were observed to harbor *Shigella.* Of these, 23 or 3.9 per cent were asymptomatic carriers. This percentage is similar to the findings of Watt, Hardy and DeCapito (1942) and Hardy and Watt (1948), who reported a carrier rate of approximately 4 per cent in Puerto Rico and in different parts of the United States. A survey among "food handlers" by Kessel and Parrish (1939) in Los Angeles showed 6.2 per cent to be positive for *Shigella.*

It is of interest to note that only 12 cases of acute shigellosis were referred from the French Colonial Hospital and Clinic for stool examination during the period of this study, while 29 acute cases of amebiasis were referred during the same time. If this difference reflects the ratio of the occurrence of acute cases of shigellosis to acute cases of amebiasis in Tahiti, then bacillary dysentery is less frequent in Tahiti than amebic dysentery. This is quite different from the prevalence rates of these two diseases in many areas.

In this survey, five persons, or 0.9 per cent of the 560 whose stools were cultured, harbored *Salmonella.* All five strains isolated were *S. anatum* which belongs to Group E. The five persons, whose ages ranged from 12 to 39 years, had no symptoms of salmonellosis. Watt and DeCapito (1950) in south Texas and Stewart and DeCapito (1953) in southwest Georgia reported surveys among children under 10 years of age in which 0.6 per cent and 0.5 per cent respectively were positive for *Salmonella.*

Levine *et al.* (1950) in Honolulu report the occurrence of 136 asymptomatic carriers of *Salmonella,* 98 of whom belonged to Group C and 17 to Group B. Adler *et al.* in Honolulu (1951) found that 13.2 per cent of dogs examined in Honolulu harbored five different types of *Salmonella.*

TABLE 2

Number of persons harboring Gram-negative non-lactose-fermenting rods

Shigella dysenteriae	6
Shigella flexneri	25
Shigella sonnei	3
Shigella newcastle	1
Total	35
Salmonella anatum	5
Proteus morgani	117
Proteus sp.	28
Pseudomonas sp.	18
Paracolon organisms	31

2. *Comparison of procedures in examining stools for intestinal protozoa*

In routine laboratory examination for intestinal protozoa, the question often arises concerning the comparative efficiency of procedures employed. Without doubt, a preliminary film in saline and preferably also iodine, e.g., d'Antoni's iodine solution, must always be employed in examining for trophozoites of intestinal protozoa. In the saline portion of the film motility is demonstrable, while in the iodine portion nuclear structure is demonstrable. The writers prefer also to make a permanent film, stained by the iron-hematoxylin method, to be used in studying more exact nuclear structure and also for a permanent record.

The zinc sulfate flotation procedure is valueless in examining for trophozoites. In examining for cysts, however, all three methods may be used. In this survey it was possible to compare the efficiency of the three procedures mentioned above, i. e., (a) preliminary direct film in saline and iodine, (b) film stained by permanent iron-hematoxylin stain and (c) zinc sulfate concentration.

These results are shown in Table 3 for a series of (a) 162 stools known to be positive for *E. histolytica*, (b) 171 stools positive for *E. coli*, (c) 226 stools positive for *E. nana*, (d) 36 stools positive for *Iodamoeba* and (e) 94 stools positive for *Giardia*.

The most satisfactory way to compare procedures of diagnosis is to select a series of stools known to be positive for cysts and to compare the several procedures to be tested on these known positive stools. It would then be possible to eliminate the personal factor in making microscopic examinations and compare only the effectiveness of the different technics employed.

It will be observed that, for the most part, higher percentages were detected by the zinc sulfate flotation procedure than by either the direct film or the film stained with iron-hematoxylin. The exceptions were for *E. histolytica* in the iron-hematoxylin stained films, in which the results equaled the results obtained with zinc sulfate, and for *Iodamoeba*, in which the iron-hematoxylin method yielded a higher percentage than the zinc sulfate flotation procedure.

Studies which include the comparative efficiency of these same methods have been reported by Faust *et al.* (1939), Tobie *et al.* (1951) and Hood *et al.* (1952). The latter two studies, however, made use of modifications of the basic methods. Consequently, they are not absolutely comparable.

TABLE 3

Percentages of positives obtained for each protozoön recorded when examined by each method listed

METHOD OF EXAMINATION	*E. histolytica* 162 POS. STOOLS	*E. coli* 171 POS. STOOLS	*E. nana* 226 POS. STOOLS	*Iodamoeba* 35 POS. STOOLS	*Giardia* 94 POS. STOOLS
	% pos.	% pos.	% pos.	% pos.	% pos.
Direct film	68	64	60	52	80
Iron-hematoxylin film	80	62	55	91	72
Zinc sulfate flotation	80	90	73	66	81

The results in this study are more nearly comparable to results obtained by Faust *et al.* (1939). In their Table II are recorded the total numbers of protozoa observed by their technics 1, 4 and 8, which are the three procedures used in the current study. For reference, Faust's results are given here in Table 4.

It will be observed in Table 4 that Faust *et al.* likewise obtained the highest percentages of positives by the zinc sulfate procedure. Their results for the two other methods were consistently lower than those in Table 3 of the current study.

Tobie *et al.* (1951) also compared the direct film and zinc sulfate concentration methods on the basis of "individuals actually infected" and concluded by their technics that the direct film method is 27 per cent efficient and the zinc sulfate concentration 59 per cent. In their study, the added factor of periodicity in occurrence of cysts in stools was also introduced.

Although the percentages of efficiency of the results obtained in these three studies i. e., Faust *et al.*, Tobie *et al.*, and the current report vary somewhat, it is of interest that all three showed the direct film to be less efficient than the zinc sulfate concentration in examining for most cysts of intestinal protozoa.

Table 5 shows the results obtained in the present study by a combination of any two of the procedures employed. It should be pointed out that results might vary in different surveys in accordance with the numbers of cysts occurring in stools.

It is seen in Table 5 that the combination of permanent iron-hematoxylin film and zinc sulfate flotation yielded the highest percentages of results for each protozoön recorded. For *E. histolytica*, in which one is most interested in laboratory diagnosis, the direct film and permanent iron-hematoxylin film yielded 96 per

TABLE 4

Results obtained by Faust (1939)

	E. histolytica	*E. coli*	*E. nana*	*Iodamoeba*	*Giardia*
No. of infections	94	130	155	16	39
	% pos.	% pos.	% pos.	% pos.	% pos.
Method 1 (Direct film)	33	55	44	19	62
Method 4 (Iron-hematoxylin)	39	63	74	31	59
Method 8 (Zinc sulfate)	69	91	71	38	87

TABLE 5

Percentages of positives obtained for each protozoön recorded when examined by any two methods listed

COMBINATION OF METHODS OF EXAMINATION	*E. histolytica*	*E. coli*	*E. nana*	*Iodamoeba*	*Giardia*
	% pos.	% pos.	% pos.	% pos.	% pos.
Direct film and iron-hematoxylin film	96	90	83	84	89
Direct film and Zinc sulfate flotation	87	93	95	84	92
Iron-hematoxylin film and Zinc sulfate flotation	100	96	97	100	96

cent, the direct film and zinc sulfate flotation 87 per cent, while the combination of permanent iron-hematoxylin film and zinc sulfate flotation yielded 100 per cent. Faust *et al.* (1939) also found this combination most efficient. Most of the cysts missed in the direct film and by zinc sulfate flotation examination were cysts under nine microns in diameter, i.e., "small race" cysts. These were later detected in the film stained with iron-hematoxylin.

3. *Complement fixation test*

Table 6 summarizes the complement fixation tests on serums from 25 individuals who were positive for *E. histolytica*. The antigen used was the aqueous antigen produced by Eli Lilly and Company and kindly provided by them. The tests were made according to their directions, using a five tube test. It will be observed in Table 6 that of 21 positive serums, 13 were from patients who exhibited acute attacks of amebiasis. Six of these were experiencing their first acute attack. Five were from individuals who exhibited chronic amebiasis only, and three from carriers. Of the four serums which were negative, three were from persons exhibiting acute attacks but who also reported chronic amebiasis symptoms for several years, and one from an individual who exhibited symptoms of chronic amebiasis only. Two of the serums which gave positive reactions were from patients who exhibited liver symptoms, one with a liver abscess and one with right upper quadrant tenderness. One of the negative serums was also from a patient having right upper quadrant tenderness in addition to his intestinal symptoms. The five control serums were negative.

The complement fixation test has produced variable results in the hands of different workers and when different antigens were employed. In the experience of the authors, the main discrepancy has been in the occurrence of false negatives. In the current series, using an aqueous extract, the serums of 16 per cent of individuals known to harbor *E. histolytica* gave negative tests, while in a previous series at the Los Angeles County Hospital, in which the Craig alcoholic-ether extract was employed, 25 per cent were negative. It is hoped that a more sensitive antigen may overcome this problem.

TABLE 6

Results of complement fixation test, using antigen supplied by Eli Lilly and Company

	Symptomatology of individuals from whom serums were tested						
TOTAL TESTED, 25	NO. WITH FIRST ACUTE ATTACK OF AMEBIASIS	NO. WITH PREVIOUS CHRONIC ATTACKS AND PRESENT ACUTE ATTACK	NO. WITH CHRONIC AMEBIASIS ONLY	NO. OF "CARRIERS" WITHOUT SUBJECTIVE CLINICAL SYMPTOMS	STAGE OF *E. histolytica* IN STOOL		
					Troph. only	Troph. and cysts	Cysts only
No. with positive tests, 21	6	7	5*	3	12	7	2
No. with negative tests, 4	0	3	1	0	2	2	0

Of five control serums from individuals negative for *E. histolytica*, all were negative.

* One individual from this group exhibited appendicitis. Trophozoites of *E. histolytica* were found in the appendix.

SUMMARY

A stool survey in which 560 individuals in Tahiti, French Oceania, were examined for intestinal protozoa, helminths and bacteria, yielded the following prevalence rates: *E. histolytica* 22.3 per cent, *Giardia* 10.0 per cent, *Trichuris* 44.0 per cent, hookworm 38.0 per cent, *Ascaris* 12.9 per cent, *Shigella* 3.9 per cent, *Salmonella* 0.9 per cent. Prevalence rates of other parasites are shown in Table 1.

A comparison of procedures used in examining stools for cysts of intestinal protozoa indicates that, for the most part, the zinc sulfate flotation procedure is more efficient than either the direct film or the film stained with iron-hematoxylin. In a comparison of the combination of any two of these methods, the iron-hematoxylin film and zinc sulfate flotation together produced the highest percentage of positives. It is emphasized that the direct film should always be used in examining for trophozoites.

The complement fixation test for amebiasis was performed on 25 serums procured from individuals harboring *E. histolytica*. Eighty-four per cent yielded positive tests. Five serums from individuals whose stools were negative for *E. histolytica* showed a negative complement fixation reaction.

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MODIFICATIONS IN VIRULENCE OF A STRAIN OF *TOXOPLASMA GONDII* BY PASSAGE IN VARIOUS HOSTS

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The various manifestations of clinical toxoplasmosis reported in man and animals (Sabin, 1942; Siim, 1951; Fankhauser, 1951; Feldman, 1953; Frenkel, 1953) attest to the possibility that *Toxoplasma* strains of varying virulence may exist in nature. Also, isolations of *Toxoplasma* from asymptomatic infections in various hosts, such as the pigeon (Jacobs, Melton and Jones, 1952) are frequently attended by difficulties resulting from the low virulence of the organisms in the early passages in laboratory animals, making the parasites difficult to detect even when their presence may be suspected. Some authors (Sabin, 1941; Frenkel, 1953) have mentioned mouse-adaptation of strains of the parasites and reported that thereafter the infections produced in mice have been uniform. On the other hand, consistent differences in behavior in mice of various strains have also been reported (Frenkel, 1953). It has also been stated that the maintenance of *Toxoplasma* in chick embryos for as many as 27 passages does not alter the virulence of the parasites for mice on intracerebral inoculation (MacFarlane and Ruchman, 1948).

In our Laboratory, differences in virulence of strains have been studied from the standpoint of several criteria. The parasitemia and antibody response produced by such strains in experimental infections in rabbits, mice and pigeons have been noted, as well as the pathogenicity for the various laboratory hosts as measured by survival or death, and by survival time. The studies on immune response will be reported elsewhere. It is proposed here to describe the origin of an avirulent strain of *Toxoplasma* and to report differences in virulence, as evidenced by parasitemia and pathogenicity, which developed in the strain as a result of passage. Some results of tests on the virulence of the RH strain after prolonged passage in chick embryos are also reported.

MATERIALS AND METHODS

The strain of parasite studied, hereinafter designated *strain 113*, was obtained in the following manner: in the course of experimental attempts at transmitting *Toxoplasma* through arthropods (Woke, Jacobs, Jones, and Melton, 1953) a number of adults of *Rhipicephalus sanguineus*, the brown dog tick, were tested for the presence of parasites by macerating their bodies in saline and inoculating the resulting suspension intraperitoneally into two mice. The particular lot of ticks in this test consisted of 45 adults which had fed 30 days previously, as nymphs, on a rabbit infected with the RH strain of *T. gondii*. The two mice showed no symptoms of toxoplasmosis. One was killed on the fourteenth day following its inoculation with the macerated ticks, and its brain, liver and spleen

[1] Laboratory of Tropical Diseases.

were ground together in saline and subinoculated intraperitoneally into two fresh mice (designated "A" mice). The following week the second of the two original mice was sacrificed, and its tissues were inoculated into the same two "A" mice which had received the first subinoculation. One of the "A" mice was sacrificed one week later, but on microscopic examination of smears of its liver, spleen and brain no toxoplasmas could be demonstrated in it. However, the second "A" mouse was examined for the presence of peritoneal exudate 16 days after its last inoculation. Fluid was found in small amount, and a few organisms identified as toxoplasmas were observed in it. The mouse was sacrificed five days later, but it was not possible, on Giemsa-stained smears of liver, spleen and brain, to confirm the earlier positive finding; therefore, further subinoculations were made.

The parasites were apparently of low virulence and it required 6 more passages, by intraperitoneal inoculation, before they were again demonstrated in the peritoneal fluid and tissues of the mice. The time between the first inoculation of the ticks into mice and this demonstration was four months, from November 29, 1950, to April 3, 1951. On April 16, 1951, after one more mouse passage, peritoneal fluid containing toxoplasmas was inoculated into 12-day-old chick embryos. Four transplants into 12-day-old embryos were made at weekly intervals, and thereafter 7-day-old embryos were used. After a total of eight transfers in chick embryos, the strain was inoculated intracerebrally into five mice, all of which survived the infection. It was also continued in chick embryos by weekly passage.

Ten days after inoculation, some of the intracerebrally inoculated mice were sacrificed and their brains used as inocula for a second intracerebral passage and for intraperitoneal inoculation of other mice. Thereafter, this strain has been transferred in mice by both these routes of inoculation, and the lines have been kept separate. They have been designated 113-IC for the intracerebral passages, 113-IP for the intraperitoneal passages; and the chick embryo-passaged line is 113-CE.

In all of these hosts, especially in the early passages, the parasites were not always demonstrable at the time of transfer, but they were subinoculated regularly nevertheless, and are now easily seen.

For the intracerebral passages, the brain of the previously infected mouse is macerated in saline, and 0.02 ml. of the suspension is inoculated into the brain of mice under ether anesthesia.

For the first intraperitoneal passages, the brain, liver and spleen of the previously infected mouse were ground together in saline, and 0.5 ml. of the resulting suspension was used as the inoculum. Later, after toxoplasmas became readily seen in the peritoneal exudate of such mice, the technic of passage was altered; the inoculum now consists of 0.1 to 0.2 ml. of a 1:40 dilution of peritoneal exudate from mice of the previous passage.

For the chick embryo passages, the chick membranes are similarly triturated in saline and 0.1 to 0.3 ml. of the suspension is inoculated directly into the yolk sac of the fresh embryos; penicillin and streptomycin, 500 units and 5 mgm. per ml. respectively, are added to the suspension in this case to insure against bacterial contamination.

Experimental work on the virulence of strain 113 has been done mostly as comparisons, in mice, of the chick embryo-passaged line (CE) and the line passed weekly or more frequently by intraperitoneal inoculation (IP). Mice were inoculated intraperitoneally with counted numbers of parasites or with progressive dilutions of macerated membranes or peritoneal fluid respectively. Counts of parasites in peritoneal fluid were made by the use of a Neubauer-Levy counting chamber and appropriate dilutions of peritoneal exudate. For counts of toxoplasmas liberated from tissues, such as chick embryo membranes or mouse brains, the tissues were macerated in saline and allowed to stand until the coarse particles were sedimented; the counts were then made on dilutions of the supernate. The inoculum was generally 0.25 or 0.5 ml. of the prepared suspensions. The number of deaths and the time of survival of animals so inoculated were noted. Studies of the parasitemia found in mice and rabbits infected with the parasites of the embryo-passaged line were performed in the manner described previously for our work on the parasitemia produced by the RH strain of *Toxoplasma* (Jacobs and Jones, 1950).

Mice of the general purpose NIH strain were used routinely in the maintenance of strains. They were received directly after weaning and weighed between 13 and 20 grams at the time they were used. For the comparative tests, a smaller range in weight of the same mice was chosen, 15 to 18 grams.

RESULTS

The results presented below describe, first, a change in the virulence of the mouse-passaged (IP) line of strain 113, as observed in the mice used for the routine maintenance of this line. A comparison of infections with 113-IP and 113-CE in rabbits, guinea pigs and hamsters is presented as evidence of the divergence of these two lines of the strain. Data on parallel tests of the pathogenicity in mice of these lines are also given, together with cumulative results of tests on the survival time of mice infected with 113-IP and 113-CE toxoplasmas, as compared with RH toxoplasmas. Further, observations on the lack of cross-immunity of these strains are mentioned and on the differences in parasitemia produced by them in experimental animals. Some differences in the course of toxoplasmosis in mice infected with 113-IP and 113-CE are also recorded. Finally, data are given on the virulence of 113-IC, the line of the strain passaged intracerebrally in mice, and a demonstration is presented that the modifications in virulence observed probably are the result of changes in the parasites themselves rather than of the presence of any concomitant infection.

The virulence of strain 113-IP gradually increased on continued passage in mice. The mice originally inoculated intraperitoneally, from the brains of mice of the first intracerebral passage after chick embryo cultivation, manifested no symptoms of disease. On the 8th day after inoculation, a small amount of peritoneal exudate was obtained on paracentesis, and a few toxoplasmas were seen in it. On the 10th day, these mice were sacrificed, and a suspension of their brain, liver, and spleen was inoculated into a second group of fresh mice. One month later, a similar passage was made. After another month, the same procedure was repeated. This fourth passage resulted in the death of one mouse on day 14;

the remaining mice were sacrificed, and a fifth passage was performed. A sixth passage was done 10 days later, and thereafter the passages were routinely performed at weekly intervals, without regard to the demonstrability of the infection in the mice.

The seventh through the ninth passages were characterized by the production of peritoneal exudate in which only a very few toxoplasmas could be seen on microscopic examination. After the ninth passage, transfers were done using a 1:10 dilution of the exudate in saline. Mice of the 10th, 11th, and 12th passages died one week after inoculation. The 13th and 14th passages were done using material from mice inoculated five days previously, before they showed signs of illness. Mice of the 14th passage died five days after inoculation. However, mice of the 15th passage were still alive at one week, and those of the 16th transfer died at one week. Thereafter, deaths began to occur more rapidly, so that the routine of transfer had to be modified. Since the 20th passage, in which the peritoneal exudate was rich in toxoplasmas, the transfers have been performed routinely twice weekly. After the 27th passage, the dilution of peritoneal exudate used in making the transfers was changed to 1:40 instead of 1:10.

The original strain, when first isolated, was nonpathogenic for rabbits, guinea pigs, hamsters and mice. After 44 passages by the intraperitoneal route in mice, 1,500 to 5,000 toxoplasmas of this line were inoculated intradermally into each of six rabbits. All these rabbits died in six to seven days. On the other hand, eight rabbits survived inoculation with similar numbers of strain 113 which had been passaged for one year, 52 transfers, in chick embryos. Since that time, numerous rabbits have been inoculated by various peripheral routes with 113-CE toxoplasmas for various studies, and all but one have survived; the one death was not due to toxoplasmosis.

Line 113-IP, tested one year or longer after passage in mice, similarly was found virulent for guinea pigs and hamsters, while 113-CE failed to produce death in guinea pigs when given in similar numbers. In hamsters, 100 toxoplasmas of strain 113-IP produced death in 8 to 20 days, while a similar inoculum of 113-CE produced no deaths. One thousand toxoplasmas of 113-IP killed all

TABLE 1

Comparison of the virulence of two lines of strain 113 of Toxoplasma gondii

INOCULUM		NO. OF MICE DEAD*	SURVIVAL TIME (DAYS)
Line	No. parasites		
IP	10	5	5, 7, 7, 8, 8
IP	100	3	7, 7, 7
IP	1,000	5	7, 7, 7, 8, 8
IP	10,000	5	6, 6, 6, 7, 7
CE	10	0	—
CE	100	1	20
CE	1,000	1	18
CE	10,000	1	more than 30

* 5 mice were inoculated in each group.

of 13 hamsters inoculated in 7 to 15 days, while the same number of 113-CE parasites killed 11 of 25 hamsters in 20 to 38 days.

Differences in virulence of IP and CE lines of strain 113 were measured on the basis of pathogenicity to mice approximately one year after the original isolation. This was after 62 passages intraperitoneally in mice and 56 passages in the chick embryo. The results of these tests are shown in Table 1.

An attempt was made at the same time to describe the differences in pathogenicity on the basis of survival time of mice inoculated with an LD_{50} dose of toxoplasmas as determined by results of inoculation of progressive dilutions of the infective material. These results are presented in Table 2. Because the dilutions were not carried out far enough, it is not possible from the data to calculate the LD_{50} inocula. Nevertheless, the data are interesting in that they demonstrate the remarkable regularity of results with the mouse-passaged line versus the irregularity of the deaths of mice inoculated with toxoplasmas derived from the chick embryo. Counts and calculations of original concentrations of parasites in the materials used showed approximately 315×10^6 toxoplasmas per ml. of the peritoneal exudate and 5×10^6 toxoplasmas per ml. of the chick membranes. Consequently, the inocula of peritoneal fluid diluted 10^{-3} and 10^{-4} are roughly comparable with the dilutions of 10^{-1} and 10^{-2} of chick membranes respectively, with less than a two-fold difference existing between the compared preparations.

In a later experiment, done approximately six months after those just reported, a wider range in dilutions was employed. The results are reported in Table 3.

Obviously, strain 113-IP increased considerably in virulence on continued passage through mice, while strain 113-CE was of much lower pathogenicity. Not only did the embryo line cause considerably fewer deaths, but the survival time of mice with fatal infections was much longer than that of similar mice infected with 113-IP. While no direct comparison of strain 113 with the RH strain was performed, the data in Table 4, gathered from a number of experiments, will serve to emphasize the present similarity of 113-IP to RH and the dissimilarity of 113-CE. The data in these experiments were obtained six months or longer after the maintenance of strain 113 by the various passage techniques

TABLE 2

Comparison of the virulence of two lines of strain 113 of T. gondii, *by dilution technique*

DILUTION	MOUSE LINE (113-IP)		CHICK EMBRYO LINE (113-CE)	
	No mice dead*	Survival time (days)	No. mice dead*	Survival time (days)
10^{-5}	5	6, 6, 7, 7, 7	3	17, 19, 21
10^{-4}	5	6, 6, 6, 6, 7	2	14, 20
10^{-3}	5	5, 5, 5, 6, 6	0	—
10^{-2}	5	5, 5, 5, 5, 5	2	17, 81
10^{-1}	5	4, 4, 4, 4, 4	3	10, 10, 10

* 5 mice were inoculated in each group.

TABLE 3

Comparison of the virulence of two lines of strain 113 of T. gondii, *by dilution technique*

DILUTION	MOUSE LINE (113-IP)		CHICK EMBRYO LINE (113-CE)	
	No. mice dead*	Survival time (DAYS)	No. mice dead*	Survival time (days)
10^{-9}	0	—	0	—
10^{-8}	2	8, 9	1	12
10^{-7}	5	7, 7, 8, 9, 9	0	
10^{-6}	5	6, 7, 7, 7, 8	2	19, 21
10^{-5}	5	6, 6, 6, 7, 8	1	12
10^{-4}	5	6, 6, 6, 6, 6	3	12, 13, 19
10^{-3}	5	4, 5, 5, 5, 5	3	17, 23, 44
10^{-2}	5	4, 5, 5, 5, 5	3	8, 15, 25
10^{-1}	5	3, 4, 4, 4, 5	5	7, 8, 16, 17, 24

* 5 mice were inoculated in each group.

described, following the original chick embryo inoculations. It is readily seen that strain 113-IP is very similar in virulence to the RH strain, while line 113-CE has been maintained at a considerably lower level of pathogenicity for mice.

Experimental work on the immunity conferred in mice by the inoculation of strain 113-CE has revealed that in general this immunity is limited to a slight prolongation in survival time over controls when challenge is made with the RH strain. In order to see if any greater degree of immunity could be produced in mice by strain 113, animals surviving an original infection with 113-CE were inoculated with 113-IP. The great divergence in strains is evidenced by the results of these tests. Thus, of 30 mice inoculated with 1,000 toxoplasmas of strain 113-CE 5 weeks previously, 30 succumbed to a challenge inoculum of 1,000 parasites of strain 113-IP. On the other hand, only one mouse of another 30 which survived the same original inoculum, succumbed to challenge with 113-CE.

Information on the parasitemia in pigeons produced by strain 113-CE and 113-IP has already been published (Jacobs, Melton and Cook, 1953). No studies on the parasitemia in rabbits infected with 113-IP have been performed, but because of the virulence of this strain and the rapid death of the animals, it is believed that they would exhibit the same high parasitemia found in rabbits infected with the RH strain. On the other hand, in a group of five rabbits infected with strain 113-CE, only one death occurred, and this death was not attributable to *Toxoplasma* infection. Samples of blood were taken from these rabbits on various days during the first three weeks following inoculation. In one rabbit, a low parasitemia was found on day 5, in another on days 5 and 7, and in a third on days 5, 7, and 9. By low parasitemia it is meant that 0.5 ml. of whole blood from these animals produced infection when inoculated into mice; dilutions of the blood did not do so. No parasitemia was found in the remaining two rabbits or on days 3, 11, 13, 15, 17, or 20 in those found positive.

Similarly, strain 113-CE produced only a transient low parasitemia in two of eight mice infected intraperitoneally or intravenously with 300 parasites. One

TABLE 4

Cumulative data from a number of experiments on survival of mice inoculated with strain 113 toxoplasmas as compared to RH parasites

NO. OF TOXOS	STRAIN AND LINE	NO. MICE DEAD / NO. INOC.	SURVIVAL TIME (DAYS), AVERAGE & (RANGE)
100	RH	60/60	7.7 (7–10)
	113-IP	25/25	6.9 (6–10)
	113-CE	56/193	23.8 (11–42)
1,000	RH	33/33	7.3 (7–11)
	113-IP	29/29	6.6 (6–9)
	113-CE	40/140	21.1 (13–37)
10,000	RH	5/5	less than 7
	113-CE	27/40	16.2 (8–30+)

half of a milliliter of a 1:10 dilution of blood drawn from these mice on day 6 and day 11 produced infections in recipient animals; on 8 other days during the first three weeks of infection the blood was negative. On the other hand mice infected with 113-IP showed parasitemias like those reported previously for RH-infected mice (Jacobs and Jones, 1950) with dilutions up to 1:1,000 of whole blood found infectious. Three baby chicks infected intravenously with 300 toxoplasmas of strain 113-CE failed to show a parasitemia.

One very definite difference between strain 113-CE and 113-IP can be expressed qualitatively here. In mice infected intraperitoneally with 113-CE, a peritoneal exudate is evident one to two weeks after infection; toxoplasmas are only rarely seen in this fluid. As the infection progresses, the exudate is no longer seen and animals which die late in the infection succumb to an encephalitis. The encephalitis is manifested by circling movements, abnormal head positions, and spasticity. Toxoplasmas are rare in impression smears made of the liver and spleen of such animals, but are easily found within the brain. On the other hand, mice infected with strain 113-IP uniformly show a peritoneal exudate rich in toxoplasmas, and the animals die of an acute generalized infection rather than of central nervous system disease. In this respect, the symptoms produced by strain 113-CE are similar to those described by Frenkel (1951) in hamsters infected with the RH strain and treated with sulfadiazine to prevent death early in the infection.

Strain 113-CE is lethal to chick embryos. The results following inoculation of 7-day-old embryos with graded doses of this line are presented in Table 5. All of the embryos inoculated with 1,000 or more toxoplasmas succumbed before the normal hatching time. Only one embryo inoculated with 100 toxoplasmas was able to hatch, and did so on the 23rd day. Three other embryos inoculated with this number of toxoplasmas survived to the 22nd or 23rd day of incubation but failed to hatch and died within the shell. Thus, although the parasites maintained within the chick embryos are relatively of low pathogenicity for mice, they nevertheless do kill the chick embryos.

Data are also available on the virulence of the intracerebrally passaged line of strain 113 (113-IC). After the first five passages during which deaths occurred

TABLE 5

Results of inoculation of 113-CE toxoplasmas into the yolk sac of 7-day-old chick embryos

NO. OF TOXOS INOC.	EMBRYOS				
	No. inoc.	No. died	No. hatched	Survival time (days)	
				Average	Individual
100	6	5	1	14.2	12, 12, 15, 16, 16
1,000	6	6	—	10.3	9, 9, 10, 10, 12, 12
10,000	6	6	—	8.7	8, 8, 9, 9, 9, 9
100,000	6	6	—	8	8, 8, 8, 8, 8, 8

TABLE 6

Results of intraperitoneal inoculation of 113-IC toxoplasmas into mice

NO. OF TOXOS	NO. OF MICE DEAD / NO. INOC.	SURVIVAL TIME (DAYS)	
		Average	Individual*
10	10/10	10.9	9 (2), 10 (4), 11, 12, 14 (2)
100	10/10	10	9 (2), 10 (6), 11 (2)
1,000	10/10	9.1	7, 8 (4), 9, 10 (3), 13
10,000	10/10	7.3	7 (7), 8 (3)

* Numbers in parentheses refer to number of mice which survived for the designated number of days.

at about one week after inoculation, this line was transferred routinely, generally every four to six days. There were a few longer intervals between passages resulting from the use of small inocula, with consequent failure of some of the mice to die, but the majority of transfers was made at four or five days. This line appeared highly virulent for mice, but in order to judge its pathogenicity on the same basis used for the other lines of the strain, it was also tested by the intraperitoneal inoculation into mice of counted numbers of parasites from brains of mice in the 113-IC series. The results are shown in Table 6.

It appears, from these data, that the intracerebrally passaged line of strain 113 was not quite as virulent as that maintained by intraperitoneal passage. While all mice inoculated with even small numbers of 113-IC succumbed to toxoplasmosis, the survival time was several days longer than that of mice infected with similar numbers of 113-IP toxoplasmas.

The possibility that the increase in virulence of 113-IP was due to a concomitant viral or bacterial infection required consideration in order definitely to establish the basis for the difference between the two lines of the strain. In order to test this possibility, two procedures were used. First, a 1:40 dilution of peritoneal exudate from strain 113-IP mice was inoculated intraperitoneally into a rat. Thirteen days later, the rat was sacrificed and portions of its brain, liver and spleen were macerated together in saline and inoculated intraperitoneally into mice. After six days, peritoneal exudate from these mice was inoculated into another group of mice. These latter mice, and those in subsequent

passages, died of toxoplasmosis in four to five days. Inocula of 10, 100, or 1,000 organisms from the peritoneal fluid of these mice killed fresh mice in the same time as did similar inocula of 113-IP.

The second test was performed as follows: peritoneal exudate from 113-IP mice was diluted so as to yield a final concentration of 4,000 toxoplasmas per ml. Mice were inoculated with 0.25 ml. amounts of this suspension, and the remainder of the material was frozen and thawed three times, with the use of dry ice, to destroy the toxoplasmas. The frozen and thawed suspension was then used as diluent in the preparation of a similar suspension of 4,000 toxoplasmas of 113-CE per ml. Another series of mice was inoculated with 0.25-ml. aliquots of this second suspension and a third series with 1,000 toxoplasmas each from a suspension of 113-CE parasites in 10 per cent serum-saline. Other mice were inoculated with the frozen and thawed suspension alone. Because of the difficulty of maintaining sterile precautions during all the manipulations in the preparation of these suspensions and because some bacteria may be present in the peritoneal exudate of mice, the mice of these groups were treated with penicillin and streptomycin daily for seven days following the inoculation. The doses of antibiotics administered were 125 units of penicillin and 1.25 mg. of streptomycin. Two groups of mice, one infected with 113-IP and one with the frozen and thawed fluid alone, were not treated with antibiotics and served as controls on this part of the procedure. The results are tabulated in Table 7.

On the basis of these data, it is believed that the difference in virulence of strains 113-IP and 113-CE is not due to a concomitant infection in 113-IP mice. The difference appears to be due to an increase in the virulence of the mouse-passaged line rather than to a diminution resulting from modifications experi-

TABLE 7

Experimental demonstration that the higher virulence of 113-IP toxoplasmas is not due to a concomitant viral or bacterial infection

INOCULUM		FLUID	ANTIBIOTIC TREATMENT	NUMBER OF MICE INOCULATED	NO. MICE DEAD	AVERAGE SURVIVAL TIME (DAYS)
Number	Line					
1,000	113-IP	serum-saline	No	10	10	7.6 (Range 7-8)
1,000	113-IP	serum-saline	Yes	10	10	8.3 (Range 8-11*)
1,000	113-CE	serum-saline	Yes	10	1	17
1,000	113-CE	frozen and thawed exudate of 113-IP	Yes	10	1	20
Frozen and thawed suspension of 4,000 113-IP toxos per ml.			No	10	0	
Frozen and thawed suspension of 4,000 113-IP toxos per ml.			Yes	10	0	

* All but one mouse died on day 8.

TABLE 8

Comparison of chick embryo- and mouse-passaged lines of the RH strain of T. gondii *as to virulence for mice*

NO. OF TOXOS INOC.	LINE	NO. MICE DEAD PER NO. INOC.	SURVIVAL TIME (DAYS)	
			Average	Individual
10	CE	9/9	8.3	8, 8, 8, 8, 8, 8, 9, 9, 9
10	Mouse	10/10	8.2	8, 8, 8, 8, 8, 8, 8, 9, 9
100	CE	9/9	8.0	7, 8, 8, 8, 8, 8, 8, 8, 9
100	Mouse	10/10	7.7	7, 7, 7, 8, 8, 8, 8, 8, 8
1,000	CE	10/10	7.7	7, 7, 7, 8, 8, 8, 8, 8, 8
1,000	Mouse	10/10	7.0	7, 7, 7, 7, 7, 7, 7, 7, 7

enced by the toxoplasmas as a result of continued passage in the chick embryo. The latter method of strain maintenance has in reality kept the parasite at a level of virulence similar to that found when the strain was originally isolated. Transfer of the RH strain of *T. gondii* in chick embryos in this Laboratory for over two years resulted in no appreciable change in its behavior in mice, as is demonstrated by the data in Table 8.

DISCUSSION

Although the majority of infections with *Toxoplasma* in nature are asymptomatic, and the parasite strains presumably of low virulence, the bulk of laboratory work on this parasite has been performed with highly pathogenic strains. This is, of course, the consequence of the isolation of these strains from acute cases of animal and human disease. Also, it appears that the usual technique of maintenance of *Toxoplasma* in the laboratory, by passage in mice, may result in augmentation in the virulence of strains.

The mechanism by which alteration in the virulence of strain 113 has occurred on murine passage cannot yet be identified. It may be that a sudden change has occurred in the ability of the parasite to destroy the cells of the host. Such a modification was reported by Sabin and Olitzky (1937) in their description of strains isolated from guinea pigs. They reported that the parasite seemed to be capable of destroying cells even before multiplication had taken place to the extent that the cells were enlarged and distended. This direct observation has not been made here, but the considerable increase in free parasites in the peritoneal exudate which we have observed along with the development of increased virulence may possibly be attributable to the same phenomenon.

Whether or not these modifications are the result of a fortuitous change in the strain, or are reproducible by repetition of the same procedures, must await further study. An investigation on this point is already in progress, but whatever modifications may occur are certainly not to be expected rapidly. Other points which must be investigated involve measurements of the reproductive rate and of the possible presence of histolytic agents in various strains.

The maintenance of the avirulent strain in chick embryos is certainly a much

simpler technique than in mice. The organisms are easily recoverable in numbers adequate for counting and preparing standardized inocula, while in mice with latent infections it is sometimes possible to find the parasite only by subinoculation. The strain itself is very valuable in that it allows study of the immunologic and serologic response of hosts which succumb in too brief a time when infected with more virulent parasites. It also allows an opportunity to study latent and chronic infections and factors responsible for variations in the susceptibility of different hosts and strains of hosts.

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A COMPARISON OF THE ANTIMALARIAL EFFECTS OF SUPPRESSIVE DOSES OF CHLOROQUINE, AMODIAQUIN, AND PYRIMETHAMINE

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The 4-aminoquinoline antimalarial, chloroquine (Aralen), has been shown by Wallace (1949) and others to be highly effective in the suppressive prophylaxis of malaria. Amodiaquin (Camoquin), a closely related drug, is also considered to be very effective (Chaudhuri *et al.*, 1952), but has not been tested as extensively. Pyrimethamine (Daraprim), an antimalarial belonging to an entirely different chemical class, has been more recently introduced into the field of malaria chemoprophylaxis, and while early reports by Vincke (1952), Canet and Farinaud (1952) and Coatney (1952) indicate a high degree of efficiency for this drug, further studies are required before an adequate evaluation is possible. The present study was undertaken to evaluate the comparative effects of chloroquine, amodiaquin and pyrimethamine in the suppressive prophylaxis of malaria.

MATERIALS AND METHODS

The study was made in Marshall Territory of Liberia, West Africa, where hyperendemic malaria, preponderantly *Plasmodium falciparum*, is present throughout the year. The subjects were 148 African school children ranging in age from 6 to 14 years. For purposes of the experiment they were divided into four groups as follows:

Group A—included 49 children with an average age of 9.4 years; each child received 12.5 mgm. pyrimethamine[1] weekly.

Group B—included 36 children with an average age of 11.2 years; each child received 0.15 gm. chloroquine (base)[2] weekly.

Group C—included 36 children with an average age of 11.0 years; each child received 0.2 gm. amodiaquin weekly.

Group D—included 27 children with an average age of 8.4 years; these children received placebos weekly, and served as controls.

Prior to drug administration, a thick blood smear from each child was examined and the malaria parasite rate determined; no slide was considered negative until at least 150 fields were studied, and if a doubtful parasite was seen an additional 150 fields were examined. A spleen survey was also made: the spleen rate was determined and the average enlarged spleen calculated (measurements of Hackett). All children then received the appropriate drug at weekly intervals with precautions to assure the swallowing of the drug in each case; at the same time a thick blood smear was taken for microscopic examination. At 4-weekly intervals the spleen examination was repeated. The study covered a period of 12

[1] Supplied through the courtesy of Burroughs, Wellcome and Company.

[2] Supplied through the courtesy of Winthrop-Stearns Inc.

weeks from August to November 1953, and was discontinued only because the lengthy annual school vacation intervened.

RESULTS

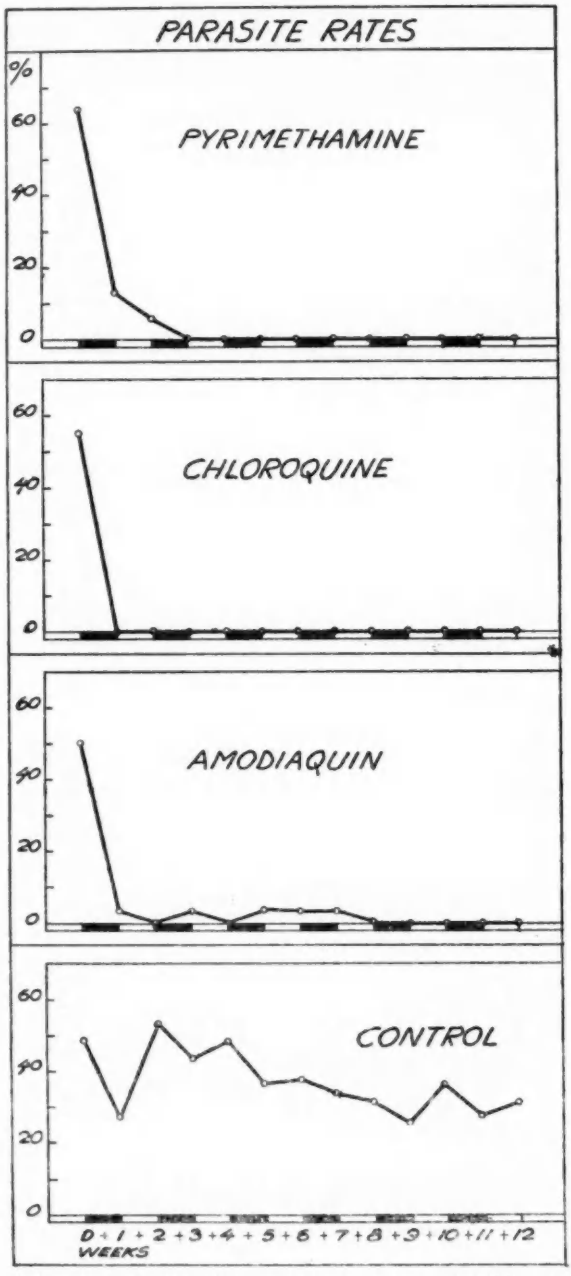
Asexual parasite rates. The parasite rates in the four groups of children under study are recorded in Table 1 and Graph 1. A study of the table shows an initial parasite rate in the different groups which ranged from 48 per cent to 63 per cent, and that all three drugs when administered at weekly intervals in the dosages indicated were effective in eliminating the asexual parasites, or reducing their numbers to a point where they could no longer be found by our method of examination. Chloroquine showed the most rapid action, and the week following the administration of a single dose of 0.15 gm. the blood of all children in group B was found free from parasites and remained negative during the course of the experiment. Amodiaquin did not appear to be quite as effective, and during the course of drug administration three different children in group C receiving this drug showed malaria parasites in their blood: two showed parasites on a single occasion each, while the third continued to show them for three consecutive weeks, after which the blood became and remained negative. None of the three children missed receiving the weekly tablet of amodiaquin. Pyrimethamine was somewhat slower in its action, and it was not until the third week of drug administration that all children in group A were found negative for malaria parasites. However, from that time the blood of all children remained negative for malaria

TABLE 1

Asexual parasite rates (P. falciparum) *in three groups of children receiving weekly suppressive doses of pyrimethamine, chloroquine, and amodiaquin*

		WEEK OF EXAMINATION											
		D*	+1	+2	+3	+4	+5	+6	+7	+8	+9	+10	+11	+12
Group A Pyrimethamine	Number examined	49	43	47	44	46	47	43	43	41	38	40	38	38
	Number positive	31	5	1	0	0	0	0	0	0	0	0	0	0
	Per cent positive	63	12	2	0	0	0	0	0	0	0	0	0	0
Group B Chloroquine	Number examined	36	35	36	34	34	35	34	34	35	35	36	36	35
	Number positive	20	0	0	0	0	0	0	0	0	0	0	0	0
	Per cent positive	56	0	0	0	0	0	0	0	0	0	0	0	0
Group C Amodiaquin	Number examined	36	31	35	32	35	34	34	34	33	33	31	30	34
	Number positive	18	1	0	1	0	1	1	1	0	0	0	0	0
	Per cent positive	50	3	0	3	0	3	3	3	0	0	0	0	0
Group D Control	Number examined	27	22	24	21	23	24	18	22	21	19	18	14	19
	Number positive	13	6	13	8	11	9	7	8	7	5	7	4	6
	Per cent positive	48	27	54	43	48	38	39	36	33	26	39	29	32

* The parasite rates indicated in this column alone include both asexual and sexual parasites, and refer to rates present at the start of drug administration.



GRAPH 1. Malarial asexual parasite rates in three groups of children receiving weekly suppressive doses of pyrimethamine, chloroquine and amodiaquin.

TABLE 2

Gametocyte rates (P. falciparum) *in three groups of children receiving weekly suppressive doses of pyrimethamine, chloroquine, and amodiaquin*

TEST GROUP	WEEK OF EXAMINATION												
	D*	+1	+2	+3	+4	+5	+6	+7	+8	+9	+10	+11	+12
Group A (Pyrimethamine)	4	9	4	2	0	0	2	0	0	0	0	0	0
Group B (Chloroquine)	3	0	6	0	0	0	0	0	0	0	0	0	0
Group C (Amodiaquin)	8	3	0	0	0	0	0	0	0	0	3	0	0
Group D (Control)	0	0	0	5	0	5	10	5	5	0	0	0	5

* The gametocyte rates presented in this column refer to those present at the start of drug administration.

TABLE 3

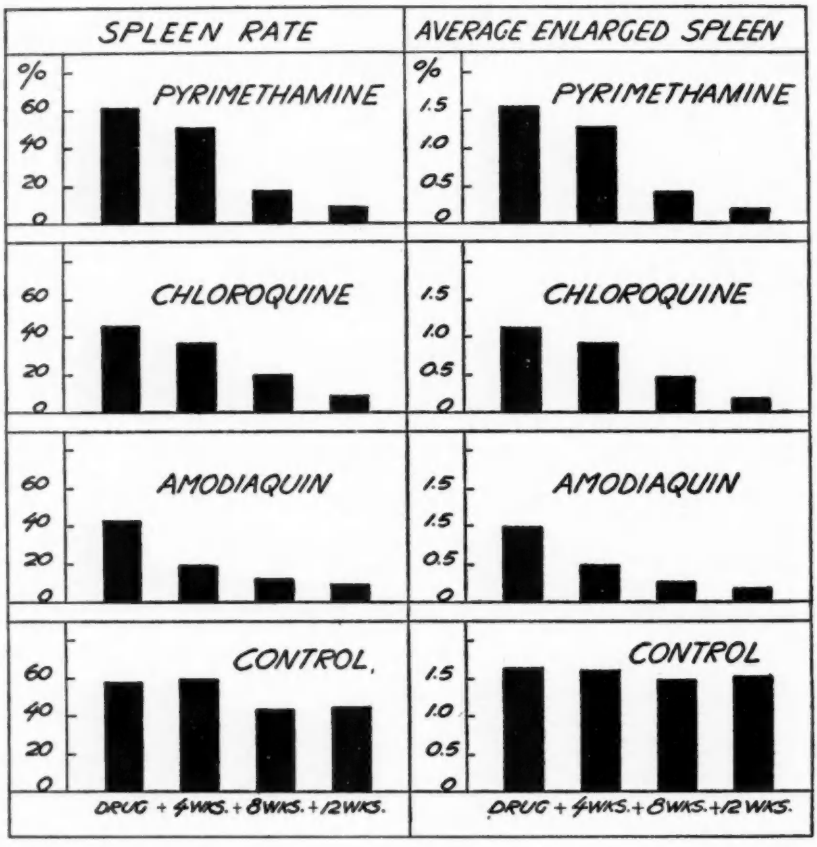
Spleen rates and average enlarged spleen in three groups of children receiving weekly suppressive doses of pyrimethamine, chloroquine, and amodiaquin

		PRE-DRUG	+4 WEEKS	+8 WEEKS	+12 WEEKS
Group A	Spleen rate	60.5	50.0	17.0	7.9
Pyrimethamine	A. E. S.	1.5	1.3	0.4	0.2
Group B	Spleen rate	45.7	37.1	19.4	8.3
Chloroquine	A. E. S.	1.2	0.9	0.4	0.2
Group C	Spleen rate	42.9	19.4	12.1	8.8
Amodiaquin	A. E. S.	1.0	0.5	0.2	0.2
Group D	Spleen rate	58.3	59.0	42.9	44.4
Control	A. E. S.	1.7	1.6	1.4	1.5

throughout the course of the experiment. The children in group D, the control series, continued to show a relatively high parasite rate.

Gametocyte (crescent) rates. The gametocyte rates in the children under study are presented in Table 2. A study of the table shows that only pyrimethamine appeared to have an immediate influence on gametocyte production, when the rate was found doubled one week after each child received one 12.5 mgm. dose of this drug. However, the rate quickly fell and gametocytes were found on only one occasion from the fourth to the twelfth week of the experiment. Gametocytes were definitely more rare in the treated groups than in the control group, and for the last eight weeks of the study of 871 blood smears examined in the three groups receiving antimalarials, gametocytes were seen on only two slides. On the other hand, of the 155 blood smears examined over the same period of time in the control group, six slides were found positive for gametocytes.

Spleen rates and the average enlarged spleen. The results of spleen examinations are recorded in Table 3 and Graph 2. It can be seen that in all three groups receiving antimalarial drugs the spleen rates showed a marked drop by the twelfth week. Spleen regression during the first four weeks appeared to be most rapid in the children receiving amodiaquin. However, from the fourth to the twelfth week the children in groups A and B receiving pyrimethamine and chloroquine respectively, showed an accelerated rate of spleen regression, and when the



GRAPH 2. Spleen rates and average enlarged spleen indices in three groups of children receiving weekly suppressive doses of pyrimethamine, chloroquine and amodiaquin.

experiment was terminated on the twelfth week all three groups showed approximately the same greatly reduced spleen rate. The average enlarged spleen in the groups receiving antimalarials showed a trend paralleling that of the spleen rates. The children in group D who served as controls, continued to show high spleen rates and average enlarged spleen.

SUMMARY AND CONCLUSIONS

The antimalarial effects of chloroquine (Aralen), amodiaquin (Camoquin) and pyrimethamine (Daraprim) were tested respectively in three groups of African school children; a fourth group served as control. A total of 148 children were studied over a period of 12 weeks. All drugs were administered at weekly intervals in the following dosages: Chloroquine (base) 0.15 gm., amodiaquin 0.2 gm.,

pyrimethamine 12.5 mgm.; children in the control group received placebos. Blood smears for parasite rate studies were examined prior to and at weekly intervals during the course of the experiment. Spleen surveys were made before and at 4-weekly intervals during the course of the experiment. At no time was there evidence of drug intolerance.

The results of parasite rate studies clearly indicate that in the dosages used all three drugs are highly efficient in clearing the blood of asexual malaria parasites. Chloroquine showed the most rapid action, and although pyrimethamine took somewhat longer to exert its effect it was equally effective in eliminating parasites from the blood. Amodiaquin did not prove to be quite as effective and in several children a temporary "break-through" did occur.

The gametocyte rate showed an early transient rise only in children receiving pyrimethamine, an observation also made by Foy and Kondi (1952). However, there was a definite decrease in the gametocyte rate in all three groups receiving antimalarials after several weeks of drug administration.

By the end of the 12-week treatment period the children in the three groups receiving the antimalarials showed an equally marked regression in both the spleen rates and the average enlarged spleen. The initial spleen reduction appeared to be somewhat more rapid in children receiving amodiaquin.

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THE THERAPEUTIC EFFECT ON A GROUP OF SLEEPING SICKNESS PATIENTS OF A SINGLE INJECTION OF 3854 R.P. (MEL B FRIEDHEIM—ARSOBAL SPÉCIA)[1]

AUGUSTO R. PINTO

Mission for the Study and Combat of Sleeping Sickness in Portuguese Guinea

Due to the powerful trypanocidal action of 3854 R.P., the report by Monnet *et al.* (1951) on elimination of the drug, and the recommendations of the Third Meeting of the International Scientific Committee for Trypanosomiasis Research, we undertook to treat sleeping sickness patients in the first stage of the disease with one injection of Arsobal.

For therapeutic trial we selected a group of 16 patients. The dose used was 4 mg. per kg. of body weight and the maximum dose injected was 198 mg. (5.5 cc. of a 3.6 per cent solution). This dosage was well tolerated and there were no serious symptoms noted, except that one patient had a violent but temporary abdominal pain immediately following the administration of the drug.

Twenty-four hours after the injection it was not possible to demonstrate the presence of trypanosomes in any of the patients. One month after treatment we looked for trypanosomes by examining the lymphatic gland fluid and also by thick blood smear, and we also made blood cultures in patients who presented alterations of the C.S.F. All these examinations were negative. The examinations of the C.S.F. carried out on this occasion showed no increase in the number of cells which exceeded 28 per cu. mm. and no increase of the albumin which exceeded 0.25 gm. per liter.

Four months after the treatment, when the patients were observed again, all were found to be clinically cured; it was not possible to find trypanosomes in any of them and the C.S.F. showed a trend toward normal except in one of the patients whose albumin went from 0.25 to 0.30 gm. per liter and the number of cells from 9 to 13 per cu. mm.

In observations on the patients made eight months after treatment, the clinical and parasitological cure was maintained, and analysis of the C.S.F. showed a decrease in the number of cells and albumin in 12 patients, while in 4 there were slight changes as follows: from 4 cells and 0.22 gm. albumin to 7 and 0.22; from 15 and 0.22 to 12 and 0.28; from 4 and 0.25 to 8 and 0.22; and from 2 and 0.25 to 14 and 0.22.

All the patients had albuminuria before receiving treatment; fifteen with traces and one with 1.5 gm. of albumin per liter. Following the injection of Arsobal the patient who had 1.5 gm. per liter showed a reduction to 0.5 gm. and among the others there were no perceptible alterations except in one case which showed an increase to 0.2 gm.

In the observations made one month after treatment, the patient who had 1.5 gm. of albumin per liter prior to treatment showed 0.75 gm.; the one who

[1] Paper presented at the Fourth Meeting of the International Scientific Committee for Trypanosomiasis Research.

TABLE 1

Results of the examinations of the C.S.F. made before and after treatment

NUMBER OF CASES	BEFORE THE TREATMENT		1 MONTH AFTERWARDS		4 MONTHS AFTERWARDS		8 MONTHS AFTERWARDS	
	Cells	Gm. albumin	Cells	Gm. albumin	Cells	Gm. albumin	Cells	Gm. albumin
1	1	0.18	21	0.22	4	0.22	3	0.20
2	3	0.15	1	0.22	3	0.20	2	0.15
3	2	0.20	6	0.25	2	0.20	1	0.22
4	2	0.15	1	0.18	2	0.20	1	0.18
5	2	0.22	28	0.22	10	0.20	4	0.25
6	1	0.20	9	0.25	13	0.30	4	0.25
7	2	0.20	11	0.22	3	0.22	2	0.20
8	0	0.20	4	0.22	4	0.22	2	0.20
9	2	0.20	1	0.25	1	0.20	3	0.22
10	2	0.18	6	0.22	4	0.22	7	0.22
11	2	0.18	1	0.20	4	0.15	3	0.22
12	1	0.18	2	0.22	4	0.20	1	0.18
13	3	0.22	8	0.22	15	0.22	12	0.28
14	3	0.22	4	0.25	4	0.25	8	0.22
15	2	0.20	2	0.25			3	0.18
16	3	0.20	2	0.25			14	0.22

had 0.2 gm. showed only a trace, and among the others, one had 0.2 gm. of albumin, nine remained with merely a trace, and in five the urine became normal. Eight months after treatment, seven patients still showed traces of albumin and the other nine had normal urines.

The study of the peripheral blood picture made before and after treatment permitted the observation that following the administration of Arsobal there was in general a slight increase of the percentage of eosinophils. This eosinophilia, which began to manifest itself 24 hours after injection, usually increased during the following days and persisted in some of the patients for as long as one month following treatment.

The period of observation of the patients is still too short to know what the final percentage of cures will be; nevertheless, the results obtained are of such a nature as to encourage a continuation of this study, since if it should be crowned with success, it will considerably improve the possibilities of combating sleeping sickness.

SUMMARY

Favorable preliminary results were obtained in the treatment of sleeping sickness patients during the first stage of the disease with the administration of a single injection of Arsobal in a dosage of 4 mg. per kg. body weight.

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ANTIBODIES AGAINST COL-SK VIRUS IN MEXICAN SERA[1]

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Much valuable information has accumulated in recent years on the pathogenic properties of the Col-SK group of viruses in experimentally infected animals, yet the role of these viruses as the etiological agents of disease in man is still uncertain. While virus has been isolated in a few instances from human sources (Dick *et al.*, 1948; Koch, 1950; Bieling, 1952; Vivell, 1952; Verlinde *et al.*, 1952) it has usually been difficult or impossible to establish a causal relationship between the isolated virus and a well-defined clinical syndrome. On the other hand, an increasing number of workers are now in agreement that antibodies against the Col-SK group of viruses may be found in a definite percentage of sera from patients suffering from various neurotropic infections. By contrast, positive reactions occur only sporadically with sera from patients sick with other diseases or with sera from healthy individuals, except during pregnancy (Smadel and Warren, 1947; Warren, Smadel and Russ, 1949; Jungeblut, 1950; Jungeblut and Horvath, 1951; Gard and Heller, 1951; Bieling and Koch, 1952; Vivell *et al.*, 1952; Keller and Vivell, 1952; Hofman and Jungeblut, 1952).

EXPERIMENTAL WORK

Our interest in the occurrence of antibodies against Col-SK virus in Mexican sera arose in 1949 when five convalescent sera were sent to us which had been collected from children who had contracted paralytic poliomyelitis during a sharp outbreak of the disease in Saltillo, Mexico. One of these sera gave marked neutralization of Col-SK virus. This observation stimulated further inquiry and in 1951 it was arranged to make a brief on-the-spot survey of the City of Puebla and surrounding terrain. On this occasion a larger number of sera were collected from cases diagnosed as paralytic or abortive poliomyelitis, from household contacts of these cases and from healthy individuals.

Materials

The total number of sera collected was 131, including 18 specimens of polio-convalescent sera, 24 specimens of contact sera, and 89 specimens of "normal" sera. The group of 18 poliomyelitis cases had occurred in the spring or early summer of 1950 in the City of Puebla or in adjoining rural areas; in 8 of them the diagnosis was only clinical, but in the remaining 10 cases positive spinal fluid findings supported the diagnosis of paralytic or abortive poliomyelitis. All except one of these patients were under 10 years of age. The 24 contact sera were from all age groups, including siblings and parents of these cases; none of the persons in this group had shown any signs of disease except the

[1] Aided by a grant from the Sister Elizabeth Kenny Foundation.

usual complement of enteric infections. The 89 "normal" sera comprised 28 samples which had been collected from medical students, 20 to 30 years old, in the City of Puebla, and 61 samples which were obtained from apparently healthy individuals of all ages living in the village of Gorospe, a small rural settlement located about 35 miles east of Puebla City near the main highway to Vera Cruz. It should be emphasized that the survey covered two geographic areas with widely differing living conditions, i.e., one a densely populated urban environment (City of Puebla, 220,000 pop.), the other an isolated rural community (Gorospe, 563 pop.). Since Warren, Russ and Jeffries (1949) had previously found that a substantial number of sera from wild rats collected in certain areas of the United States had neutralizing antibodies against EMC virus, and since similar observations had been made in Germany and in Uganda (Africa), efforts were also made to collect rat sera in Mexico. Unfortunately, no rat sera could be obtained in the area of our survey, even though there was ample evidence of the presence of wild rats near the human habitations in Gorospe. However, we are indebted to the Instituto de Salubridad y Enfermedades Tropicales for making available to us a group of 19 sera from wild rats which had been trapped in Mexico City.

Methods

The sera were examined in New York for their ability to neutralize Col-SK virus; some were also studied for their capacity to inhibit hemagglutination by this virus. In addition, the sera from all poliomyelitis patients and contacts were tested for their content of neutralizing antibodies against Yale-SK virus (Type II). Neutralization tests against Col-SK virus were carried out by injecting young albino mice intraperitoneally with incubated mixtures of equal parts of undiluted serum and 10-fold serial dilutions of mouse brain virus, in the range of 10^{-3} to 10^{-7}. Groups of four mice were used for every level of virus tested, each mouse receiving 0.2 cc. of virus-serum mixture. Control mice were injected with mixtures of normal monkey serum in combination with corresponding virus dilutions, carried up to the endpoint of infectivity. The neutralization index was determined by comparison of the LD_{50} values in test and control mice, as computed by the Reed-Muench method. For the purpose of this study, an index of 0–99 was considered negative, an index of 100–499 as questionable, and an index of 500 or above as positive. While this evaluation probably eliminated some weakly positive sera which might have had epidemiological significance in this survey, it served to remove any doubts as to the immunological significance of the results. Tests with positive specimens were repeated following inactivation of the serum for one-half hour at 56°C. and essentially the same results were obtained. Hemagglutination-inhibition tests were carried out by combining 0.1 cc. of progressive serum dilutions with 0.1 cc. of a virus dilution equal to at least 4 hemagglutinating units, usually a dilution of 1:40. After letting the mixtures stand for one hour at room temperature, 0.1 cc. of a 0.25 per cent suspension of human 0 erythrocytes was added. Controls with virus alone and with virus in combination with normal monkey

serum accompanied each test. The use of human red cells instead of sheep red cells requires the use of potassium-veronal buffer as diluent for all reagents. This method obviates the necessity for previous absorption of the human sera for their content of heterophile hemolysins and greatly simplifies the technic of the test (Horvath and Jungeblut, 1952). The results were read after the tubes had been kept in the icebox overnight. Reactions were graded as follows: Negative = inhibition up to a serum dilution of 1:5; questionable = inhibition up to a serum dilution of 1:10; positive = inhibition above a serum dilution of 1:10. Again the criteria were more stringent than applied by others. However, because of the uncertainty attending the use of any new test, it seemed more desirable to record only clear cut reactions as positive. Neutralization tests against Yale-SK virus were carried out by injecting groups of eight young albino mice intracerebrally with 0.03 cc. of an incubated mixture which contained equal parts of undiluted serum in combination with a 10^{-1} dilution of mouse brain virus. The amount of virus was equal to at least 100 LD_{50} as shown by titration in control mice receiving mixtures of virus and of normal monkey serum. A serum was considered positive when it protected at least 6 of the 8 injected mice, equivocal when it protected 5 or 4 mice, and negative when fewer than 4 mice survived.

RESULTS

The overall results of the serum reactions against Col-SK virus are brought together in Table 1. It will be seen that polio-convalescent and "normal" sera collected in the City of Puebla gave consistently negative neutralization reactions, a few positive reactors being encountered among the household contacts of these cases. On the other hand, a substantial number of polio-convalescent and "normal" sera collected in the rural areas contained neutralizing antibodies; positive reactions were likewise obtained with the sera from some household contacts. Neutralizing antibodies in these sera frequently equalled in titer that found in convalescent sera from animals experimentally infected with Col-SK virus. Moreover, the fact that the distribution of positive neutralization reactions was in good agreement with that of positive hemagglutination-inhibition tests speaks for the specificity of these immune reactions. As far as the results of the Yale-SK neutralization tests are concerned, suffice it to say that

TABLE 1

Immune reactions against Col-SK virus with Mexican sera

PERSONS TESTED	URBAN							RURAL						
	No.	Positive		Quest.		Negative		No.	Positive		Quest.		Negative	
		N	HI	N	HI	N	HI		N	HI	N	HI	N	HI
Polio. cases	13	0	0	0	1	13	12	5	4	3	1	1	0	1
Contacts	13	3	3	1	0	9	10	11	3	4	0	1	8	6
"Normal"	28	0	0	3	0	25	28	61	16		3		42	

N = Neutralization reaction. HI = Hemagglutination-inhibition reaction.

TABLE 2

Serum reactions of inhabitants of various housing units in Gorospe

HOUSE	INHABITANT	SPECIMEN NO.	RELATION	AGE	TYPHUS FEVER		Col-SK VIRUS NEUTRALIZATION
					Clin. hist.	Weil-Felix	
I	G. P.	1	Mother	32	—	—	Negative
	E. V.	2	Son	16	1951	Pos. 1:500	Negative
	C. V.	3	Daughter	15	1951	Pos. 1:500	Questionable
	F. V.	4	Daughter	9	1951	Pos. 1:500	Positive
II	E. P.	5	Mother	40	1948	—	Positive
	M. P.	6	Daughter	22	—	—	Negative
III	T. M.	7	Sister	35	—	—	Negative
	M. M.	8	Sister	33	—	—	Negative
IV	P. G.	9	Mother	35	—	—	Positive
	J. V.	10	Daughter	16	1951	Pos. 1:500	Negative
	R. V.	11	Daughter	13	1951	Pos. 1:250	Negative
V	A. H.	12	Sister	19	—	—	Negative
	F. H.	13	Sister	13	—	—	Negative
VI	J. R.	14	Sister	35	—	—	Positive
	J. R.	15	Sister	25	—	—	Positive
VII	R. G.	16	Father	49	—	—	Positive
	P. S.	17	Mother	30	—	—	Negative
	C. G.	18	Son	11	—	—	Negative
	S. G.	19	Daughter	10	1951	Pos. 1:1000	Questionable
	E. G.	20	Daughter	5	—	—	Negative
VIII	E. P.	21	Father	38	1951	Pos. 1:1000	Negative
	L. G.	22	Mother	48	—	—	Negative
	C. P.	23	Daughter	8	1951	Pos. 1:250	Positive
	J. P.	24	Son	7	1951	Pos. 1:500	Negative
IX	J. P.	25	Father	33	—	—	Positive
	C. R.	26	Mother	25	1951	Pos. 1:1000	Negative
	C. P.	27	Daughter	7	1951	Pos. 1:250	Negative
	G. P.	28	Uncle	35	—	—	Negative
	G. R.	29	Grandfather	62	—	—	Negative
X	N. A.	30	Mother	45	—	—	Negative
	D. J.	31	Daughter	26	—	—	Negative
	A. J.	32	Daughter	20	—	—	Questionable
	G. J.	33	Son	9	—	—	Negative
	A. J.	34	Mother	30	1949	—	Negative
	A. A.	35	Son	14	—	—	Positive
	M. A.	36	Son	8	—	—	Positive
	C. A.	37	Uncle	46	—	—	Positive
	M. A.	38	Uncle	26	—	—	Negative
	M. S.	39	Grandmother	68	—	—	Negative

TABLE 2—*Concluded*

HOUSE	INHABITANT	SPECIMEN NO.	RELATION	AGE	TYPHUS FEVER		Col-SK VIRUS NEUTRALIZATION
					Clin. hist.	Weil-Felix	
XI	I. G.	40	Father	51	—	—	Negative
	S. P.	41	Mother	44	1951	Pos. 1:1000	Negative
	C. G.	42	Daughter	20	1951	Pos. 1:500	Positive
	P. G.	43	Son	16	1951	Pos. 1:1000	Negative
	H. G.	44	Daughter	12	1951	Pos. 1:500	Negative
	A. G.	45	Son	10	1951	Pos. 1:300	Negative
	I. G.	46	Daughter	6	1951	Pos. 1:500	Positive
XII	P. R.	47	Father	70	1951	Pos. 1:500	Negative
	C. R.	48	Mother	60	—	—	Negative
	A. R.	49	Daughter	35	1938	—	Negative
	J. R.	50	Daughter	17	—	—	Negative
	C. P.	51	Grandchild	25	—	—	Negative
	A. M.	52	Grandchild	17	1951	Pos. 1:500	Negative
XIII	M. J.	53	Father	50	—	—	Positive
	G. C.	54	Mother	46	—	—	Negative
	L. J.	55	Son	25	—	—	Negative
	N. J.	56	Grandchild	18	—	—	Positive
	E. J.	57	Grandchild	11	—	—	Negative
XIV	D. F.	58	Mother	45	—	—	Negative
	L. V.	59	Daughter	23	—	—	Negative
	G. V.	60	Daughter	12	1951	Pos. 1:250	Positive
	J. V.	61	Daughter	8	1951	Pos. 1:250	Negative

all of the 18 polio-convalescent sera and all of the 24 contact sera, irrespective of the area in which they had been collected, were capable of inactivating this virus.

It appears from these data that there existed a sharp difference between urban and rural sera, in general, regarding their reactivity towards Col-SK virus; this difference did not exist with respect to their reactivity towards Yale-SK virus. An effort was made, therefore, to study more fully the epidemiological factors in the rural areas which might have contributed to the high incidence of positive reactions against Col-SK virus. Of particular interest in this connection was the village of Gorospe where it had been possible to secure serum specimens from approximately one-tenth of the entire population. The inhabitants are practically all of mixed Indian and Spanish blood, interrelated by marriage, and live in small family groups under the most primitive housing conditions. Gorospe, lying in a belt of endemic typhus fever, experienced a serious outbreak of the disease in the spring of 1951. At the time of the survey there was not a single case of clinical poliomyelitis in Gorospe. However, in neighboring villages (Tepeaca, San Juan Carpinteros, Tepeyahualco), within a radius of 5–20 miles, three cases of paralytic poliomyelitis had occurred shortly before, all of which gave strongly positive serum reactions with Col-SK virus.

Since a possibility could not be denied that there might be some relationship between the mode of transmission of *Rickettsia mooseri* and that of Col-SK virus, the circumstances affecting distribution of positive serum reactions against both agents were studied among the donors. In Table 2 there are listed 14 houses with their respective inhabitants and pertinent data are given regarding the clinical histories and laboratory findings for each individual. Moreover, the frequency of positive Weil-Felix reactions and of positive Col-SK virus neutralization reactions was determined over successive age groups. The results are shown in Fig. 1.

The data presented in Table 2 offer nothing to show that positive Weil-Felix reactions and positive Col-SK virus immune reactions are related in frequency of their occurrence among the inhabitants of the various housing units. Moreover, when serum reactions of individual donors were compared, positive and negative reactions against the two viral agents did not go hand in hand. The available information, therefore, makes it unlikely that these reactions were brought about by a common environmental factor peculiar to the mode of living. It also disposes effectively of the possibility that the two agents may share a common antigen. On the other hand, it will be appreciated from Fig. 1 that the risk of exposure in various age groups is somewhat similar for both viruses. Thus, the frequency of serological responses against *R. mooseri* and against Col-SK virus shows close correlation throughout childhood and adolescence, although a secondary peak of Col-SK virus immune reactions appea-

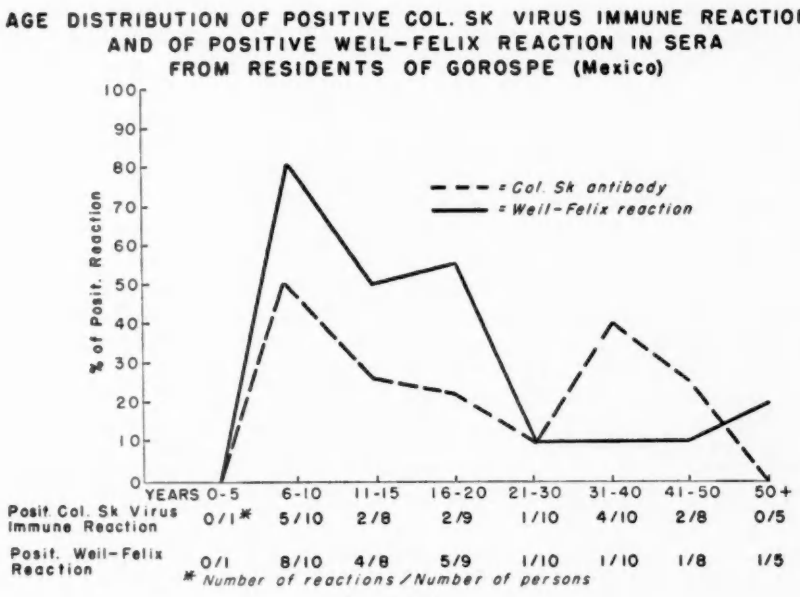
AGE DISTRIBUTION OF POSITIVE COL. SK VIRUS IMMUNE REACTION AND OF POSITIVE WEIL-FELIX REACTION IN SERA FROM RESIDENTS OF GOROSPE (Mexico)
% of Posit. Reaction
100
90
80
70
60
50
40
30
20
10
0
= Col. Sk antibody
= Weil-Felix reaction
YEARS 0-5 6-10 11-15 16-20 21-30 31-40 41-50 50+
Posit. Col. Sk Virus Immune Reaction 0/1* 5/10 2/8 2/9 1/10 4/10 2/8 0/5
Posit. Weil-Felix Reaction 0/1 8/10 4/8 5/9 1/10 1/10 1/8 1/5
* Number of reactions / Number of persons

FIG. 1

again in the older age groups which is not found with positive Weil-Felix reactions. Basing our judgment on the material at hand, it would be hazardous to draw any further conclusions until it should prove possible to demonstrate Col-SK virus or antibodies in rats which had been trapped in the same locality. Unfortunately, the fact that three positive specimens were found among 19 wild rat sera collected in Mexico City contributes nothing to the solution of the problem.[2]

DISCUSSION

It has been generally accepted until now that antibodies against the Col-SK group of viruses are rarely found in sera from healthy individuals. There is also considerable evidence that a small percentage of positive serological reactions, especially those demonstrable through inhibition of viral hemagglutination, may be obtained with sera from patients with a diagnosis of paralytic or nonparalytic poliomyelitis, so-called aseptic meningitis, and encephalitis of unknown origin. The experience of three independent sets of investigators is remarkably uniform in this respect, as shown by a breakdown of the reported figures in Table 3. Assuming the specificity of the immune response, the serological evidence, therefore, adds support to the position that the Col-SK group of viruses is capable of inducing infection in man, even though the particular type of disease produced remains to be further determined.

The data presented in this paper are of interest because they describe an unprecedented incidence of strongly positive immune reactions against Col-SK virus in human sera collected in Mexico. The occurrence of these reactions was sharply limited geographically because a significant percentage of positive reactions was found only in residents of an isolated rural settlement and not in an urban environment. Neutralizing sera were encountered in a high order of frequency with cases of paralytic poliomyelitis, their contacts, and with healthy individuals. The fact that the rural area studied was the scene of a serious outbreak of endemic typhus fever shortly before our survey adds to the interest of these observations in so far as the question of the origin of these antibodies is concerned.[3]

Further investigation failed to reveal any convincing correlation between a history of typhus fever infection and the presence of Col-SK virus antibodies in the serum of the donors. Hence, there is no compelling reason to assume that the rat was a common vehicle of transmission for both viruses. It may be said, though, that the age distribution of positive Weil-Felix reactions and of antibodies against Col-SK virus ran closely parallel through childhood and

[2] It is of collateral interest to mention here that neutralizing antibodies of high titer against Col-SK virus could be demonstrated in the serum of one of three wild Mexican monkeys belonging to the species *Ateles niger*. These animals had been captured in the vicinity of Vera Cruz.

[3] In 1952, Dr. G. Dalldorf made another survey of the same area and collected additional specimens of sera which were tested in Albany for neutralization of MM virus. The results, published in the Annual Report of the Division of Health, 1952, p. 3–5, confirm our own observations in that more than 10 per cent of the Gorospe sera were found to neutralize strongly the MM virus.

TABLE 3

Incidence of positive hemagglutination-inhibition reactions against the Col-SK group of viruses in human sera

DISEASES	GARD AND HELLER		JUNGEBLUT AND HORVATH		KELLER AND VIVELL	
	Sera No.	Positive %	Sera No.	Positive %	Sera No.	Positive %
Poliomyelitis, Aseptic meningitis, Encephalitis	384	12.5	57	16	242	12.4
Other diseases	39	0	12	0	270	3.7
Healthy individuals	146	0.7	80	2.5	133	4.5

adolescence, suggesting the operation of some common factor which determines the risk of exposure and infection.

The question as to the etiological relationship between Col-SK virus antibodies and the clinical syndrome of human poliomyelitis has been raised from time to time, a) because of the similarity in symptomatology and pathology of both experimental disease processes, b) because of the empirical demonstration of the presence of immune substances against this virus in the sera from patients with a diagnosis of poliomyelitis. The problem receives no definitive clarification from our work. In the first place, a majority of urban cases of epidemic poliomyelitis, in Mexico as well as in other parts of the world, are obviously not connected with a serological response to Col-SK virus but coincide with the presence or appearance of type-specific antibodies against the classical virus. This is further illustrated by observations of Hammon and Sather (1953) who found an unusually precocious age distribution of neutralizing antibodies against all three types of poliomyelitis virus in "normal" human sera collected from a mixed economic group in Mexico City. On the other hand, the focal accumulation of neutralizing antibodies against Col-SK virus, which was singularly characteristic of polio-convalescent and of contact sera as well as of "normal" sera in a certain rural area of Mexico, requires some explanation. It is difficult to offer a rational interpretation unless one assumes the existence of another infectious disease entity which may present a clinical syndrome similar to that of poliomyelitis but which possesses dissimilar epidemiological features. That such a disease occurs in man—for which the name "parapoliomyelitis" has been tentatively proposed—is postulated by workers in Europe who have also stressed the rural and endemic character of the infection as well as a possible connection with a rodent reservoir of the virus (Bieling and Koch, 1952). It remains for further studies to shed more light on this problem.

SUMMARY

Antibodies of high titer against Col-SK virus were found in approximately 30 per cent of a group of 77 human sera drawn from poliomyelitis cases, their contacts, or healthy individuals residing in a rural area of the State of Puebla

in Mexico. Similar antibodies were found in approximately 5 per cent of a group of 54 human sera drawn from poliomyelitis cases, their contacts, or healthy individuals residing in the City of Puebla. There was good agreement between positive neutralization reactions and positive hemagglutination-inhibition tests. The age distribution of immune reactions against Col-SK virus was unlike that of neutralization reactions against Yale-SK virus but resembled that of positive Weil-Felix reactions through childhood and adolescence.

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ISOLATION OF *SHIGELLA* AND *SALMONELLA* ORGANISMS FROM NILE FISH[1]

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Fish taken from polluted waters have rarely been found to harbor human enteric pathogens although these organisms are known to be able to survive in both fresh and salt water and it is generally agreed that the bacterial flora of fish is determined by their environment. The literature on the bacteriology of fish, as reviewed by Griffiths (1937) and Guelin (1952), contains many reports of the isolation of coliform organisms from specimens caught in polluted rivers, bays and estuaries but *Shigella* and *Salmonella* organisms have been isolated in very few instances.

Gibbons (1934) found *S. typhi* in one of 43 fish in Canada; Gohar (1934) isolated an organism belonging to the *Shigella* group in 1 of 150 fish from the Red Sea; and Arcisz (1950) recovered a strain of *S. enteritidis* from 1 of 29 Caribbean fish. *Salmonella* and other organisms have been found in prepared fish implicated in outbreaks of food poisoning, but whether the contamination occurred in nature or during preparation usually could not be determined (Brunner, 1949; Costa Mandry, 1940; Dolman, Chang, Kerr and Shearer, 1950; Edwards, Bruner and Moran, 1948; Kapsenburg, 1938; Kleeman, Frant and Abrahamson, 1942; Lodenkamper, 1952; Pivnick, 1951; Ruys, 1948; and Steiniger, 1951).

In a study of the epidemiology of gastroenteritis in Egypt particular attention has been paid to the role of food in the transmission of the etiological agents. Since fish are an important part of the diet of a major portion of the population (Barakat and Galila, 1951), and since fish have often been the suspected vehicles in outbreaks of food poisoning in this country (Azmy, 1944; Emara, Moustafa and Elyan, 1950; Fahmy, El-Kholi and Gohar, 1938; and Moustafa, Elyan and Gohar, 1948), a bacteriological survey was made of the commercially important types. That a considerable per cent of the Nile fish examined during this study harbored *Shigella* and *Salmonella* organisms is shown in the present report.

MATERIALS AND METHODS

Eleven hundred and twenty-eight freshly caught Nile fish were purchased at the Cairo municipal fish market between October, 1951, and October, 1952. Usually 15 to 20 of one or more of the commercially important types were bought on a single day. Small specimens, 15–20 cm. in length and weighing 25–75 grams, were obtained in preference to larger ones because of economy and availability.

At the laboratory the fish were sorted into pools of three of the same species. Using sterile instruments the abdominal walls were opened and 1 to 2 grams of intestinal contents were removed from each of the three and pooled in a large

[1] The opinions or assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

TABLE 1

Number of pools and distribution of positives among various species of fish

FISH*	NO. POOLS	NO. POOLS POSITIVE	PER CENT POSITIVE
Bagrus bayad	36	8	22.2
Barilius loati	34	3	8.8
Clarias lazera	40	5	12.5
Clupea finta	22	2	9.0
Hydrocyon forskalii	22	0	0.0
Labeo niloticus	32	0	0.0
Lates niloticus	33	2	6.0
Mugil cephalus	36	1	2.7
Tetrodon fahaka	7	3	42.8
Tilapia nilotica	78	15	19.2
Schilbe mystus	5	4	80.0
Synodontis schall	31	1	3.2
	376	44	11.1

* Nomenclature according to Boulenger (1907).

tube containing 25 ml. of sterile saline solution. This material was stirred with a glass rod and then allowed to stand for a few minutes to allow the gross particles to settle. Afterwards a flask containing 50 ml. of tetrathionate broth (Difco) was inoculated with 5 ml. and Shigella-Salmonella (SS) agar (Difco), MacConkey agar (Difco) and bismuth sulfite agar (Difco) plates were streaked with standard loopsful of the suspension. Following 24 hours incubation subcultures were made from the tetrathionate flask onto SS, MacConkey and bismuth sulfite agar plates.

Bismuth sulfite agar plates were incubated at 37°C. for 48 hours, all others for 24. Suspicious non-lactose-fermenting colonies were transferred to triple sugar-iron agar (Difco) slants. Cultures on this media showing reactions suggestive of *Shigella* or *Salmonella* were tested for their biochemical and physiological properties. Those having reactions characteristic of the *Shigella* group were finally identified with group and type specific sera. Those having reactions typical of the *Salmonella* group were partially identified with group sera and subsequently sent to a *Salmonella* typing center[2] for complete serological identification.

Other enteric organisms isolated from the intestinal contents were identified as far as was feasible.

RESULTS

Eleven hundred and twenty-eight fish were combined into 376 pools of 3 fish each of the same species. *Shigella* or *Salmonella* organisms were recovered from 44, or 11.1 per cent of the pools. Table 1 shows the number of pools of the different species and the number and distribution of the positive pools.

Forty-seven strains of *Shigella* and *Salmonella* were found, 3 of the positive

[2] Bacteriology Division, Naval Medical Research Institute, Bethesda, Maryland.

TABLE 2

Shigella and Salmonella organisms isolated from fish

ORGANISM	NUMBER ISOLATIONS	PER CENT TOTAL ISOLATIONS
Shigella:		
dysenteriae 1	1	2.1
dysenteriae 2	9	19.1
dysenteriae 3–7	10	21.3
flexneri 2a	2	4.3
flexneri 3	1	2.1
flexneri 5	1	2.1
flexneri 6	1	2.1
boydii 2	1	2.1
boydii 5	1	2.1
sonnei	7	14.9
	34	72.2
Salmonella:		
typhi	7	14.9
paratyphi A	2	4.3
paratyphi B	2	4.3
paratyphi C	1	2.1
ness-ziona	1	2.1
	12	27.7
Total	47	99.9

TABLE 3

Incidence of other enteric organisms in fish pools

ORGANISM	PER CENT POOLS
E. coli	100.0
Proteus	91.5
Alkaligenes	81.4
Paracolons	66.3

pools yielding 2 pathogens each. *Shigella* comprised 72.2 per cent and *Salmonella* 27.7 per cent of the total isolations. Ten strains of the Sach's group (*S. dysenteriae 3–7*), 9 of *S. dysenteriae 2*, 7 of *S. sonnei*, 2 of *S. flexneria 2a*, and 1 each of *S. dysenteriae 1*, *S. flexneri 3*, *S. flexneri 5*, *S. flexneri 6*, *S. boydii 2* and *S. boydii 5* were isolated. *S. typhi* was found in 7 pools, *S. paratyphi A* and *S. paratyphi B* were each found twice, and *S. paratyphi C* and *S. ness-ziona* were recovered once (Table 2).

The incidence of other enteric organisms in the pools is listed in Table 3. *Escherichia coli* was present in all pools, *Proteus* was found in 91.5 per cent, *Alkaligenes* in 81.4 per cent and paracolon organisms in 66.3 per cent.

DISCUSSION

The isolation of human enteric pathogens from a considerable number of the pools examined in this study is felt to be both of academic interest and public health importance. Although *Shigella* and *Salmonella* have been found previously in fish, the instances were so rare and isolated and the number of strains recovered so few that the reports could have been considered oddities. In the present study it has been shown that these organisms may be consistently found in fish taken from highly polluted waters.

The presence of the organisms in fish was not necessarily indicative of infection in the fish but it did demonstrate that fish may serve as temporary hosts for human enteric pathogens. This was of especial interest in the case of *Shigella* which has been thought to have a very restricted number of hosts in nature. In view of the repeated association of fish with outbreaks of food poisoning and the long recognized analogous situation in shellfish and oysters, the finding of *Salmonella* was not so surprising. How long *Shigella* and *Salmonella* may be harbored by fish in nature is problematical. It has been shown by Brunner (1949) that fish artificially infected with *S. enteritidis* continue to excrete the organisms for several months and perhaps for life, but this may not be true in nature where the inocula are probably smaller.

In general the number of positive pools isolated from the various species of fish reflected their reported feeding habits (Boulenger, 1907). There was a greater per cent of positives from the silurids (catfish), which are notoriously "dirty feeders" than from the other types. However, the high incidence of coliforms and other pollution indicating organisms was evidence that all the fish examined were susceptible to contamination.

Although the sampling technic did not permit an exact determination of seasonal incidence of *Shigella* and *Salmonella* organisms in Nile fish, certain trends were evident. Since the contamination of the fish was a result of widespread use of the river and irrigation canals for sewage disposal in an area of high endemicity of shigellosis and salmonellosis, most of the isolations were made during the spring and early summer when the incidence of human disease was highest. Few positive cultures were recovered from fish during the fall, when a secondary rise in the number of human cases occurred. This period coincided with the flood stage of the Nile and dilution may have been a factor.

Considering the origin of the organisms it might have been expected that the relative incidence of genera, species and types found in fish would be approximately the same as that reported from human cases. This was roughly true in the instance of *Salmonella* species, while that of the *Shigella* organisms was somewhat different (Gillmore and Watts, 1951; Floyd, 1953). This variation could possibly reflect a difference in the ability of various species and types of the latter to survive in water and fish.

The presence of human enteric pathogens in fish could result in human infection. It has been shown (Brunner, 1949; Clough and Clark, 1934; Gee, 1927; Griffiths and Fuller, 1936; Griffiths, 1937; Proctor and Nickerson, 1935; and Shewan, 1942, 1945) that bacteria rapidly migrate from the viscera into the

flesh after fish are caught. Thus, in addition to the chance for contamination of hands and other foods during cleaning, there is the possibility of deep seated organisms surviving various methods of preparation. Dolman, Chang, Kerr and Shearer, 1950; Kapsenburg, 1938; Kleeman, Frant and Abrahamson, 1942; Obst, 1919; Pivnick, 1951; Ruys, 1948; and Steiniger, 1951, have reported the survival of bacteria in the flesh of fish after cooking, pickling and smoking. This is of special importance in Egypt where fish are not refrigerated until they reach the market and where salting and rapid frying are common methods of preparation (Araman, 1941; and Khalil, 1936).

SUMMARY

1. The intestinal contents of 1128 fish, combined into 376 pools, were cultured for the presence of human enteric pathogens. *Shigella* or *Salmonella* organisms were recovered from 44, or 11.1 per cent, of the pools.

2. Thirty-four strains of *Shigella* and 13 of *Salmonella* were found. *S. typhi*, *S. dysenteriae 2* and *S. sonnei* were the organisms most commonly encountered.

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ERYTHROCYTE SENSITIZING SUBSTANCES FROM FIVE STRAINS OF LEPTOSPIRAE[1]

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One of the chief difficulties in the study of the leptospiroses has been the lack of satisfactory diagnostic facilities. The agglutination-lysis test (Schueffner and Mochtar, 1927), accepted by most workers in this field, involves the maintenance of numerous strains of leptospirae and is technically laborious. It is obvious that only a central laboratory or a research center is able to carry out the agglutination-lysis test. Several investigators have prepared leptospiral complement-fixing antigens from suspensions of leptospirae (Gaehtgens, 1933; Pot and Dornick, 1936; Carlinfanti, 1941). These antigens, however, have not gained wide acceptance. The complement-fixing antigen obtained by sonic vibration (Randall *et al.*, 1949) was reported to be as specific and as reliable as the agglutination-lysis test in the laboratory diagnosis of acute leptospirosis (Gochenour *et al.*, 1952). Ezell and co-workers (1952) stated that the soluble antigen of leptospirae was highly strain specific. At this stage, published data are not sufficient to evaluate critically the sonic vibrated and the soluble antigens.

Following the demonstration by Keogh and co-workers (1947, 1948) that the specific polysaccharide of *Hemophilus influenzae* is capable of adhering firmly to erythrocytes thereby rendering such erythrocytes agglutinable by specific antiserum, numerous workers have demonstrated the erythrocyte-sensitizing activity of many bacterial antigens (Middlebrook and Dubos, 1948; Hayes, 1951; O'Connor and MacDonald, 1950; Feinberg and Wright, 1951; Kirby 1951). In this laboratory, serologically active erythrocyte-sensitizing substances, ESS, have been isolated from rickettsiae of the typhus and Rocky Mountain spotted fever groups and the ESS test has been shown to be a specific, simple, highly sensitive and economical test for the diagnosis of the typhus and the Rocky Mountain spotted fever groups of diseases (Chang, 1953; Chang, Snyder and Murray, 1953, 1954). In view of these results with the rickettsiae, it was decided to undertake a somewhat similar chemical fractionation of the pathogenic leptospirae. In this publication, the successful isolation and the serological properties of the leptospiral-ESS are described.

MATERIALS AND METHODS

Strains. Leptospira icterohemorrhagiae (*L. ictero.*), *L. canicola* (*L. can.*), *L. pomona* (*L. pom.*), *L. hebdomadis* (*L. heb.*) and *L. autumnalis* (*L. aut.*) were obtained through the courtesy of Miss Julia M. Coffey, Division of Laboratories and Research, N. Y. State Department of Health. The leptospirae were grown by inoculating 1 ml. of a mature culture, usually 7 to 14 days old, into 20 ml. of

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Stuart media containing 10% inactivated rabbit serum (Stuart, 1946). The media were incubated at 30°C. for about two weeks. The leptospirae were harvested from the culture by centrifugation at 10,000 r.p.m. for 30 minutes at 20 to 25°C. in a Sorvall angle head. The sedimented leptospirae were resuspended in sufficient 0.85% NaCl solution to give an optical density of 0.25 at a wave length of 650 milli-microns in the 18 mm. cuvette of a Junior Coleman spectrophotometer. This procedure standardized the number of leptospirae per ml. of diluent. The leptospirae were thus concentrated about 10 to 40 fold. Occasionally certain batches of leptospirae failed to resuspend evenly after the high speed centrifugation; such batches were not included in comparative studies.

Antisera. Rabbit anti-leptospira sera were prepared by immunizing rabbits with live leptospira cultures (Ezell *et al.*, 1952). All rabbit sera used in this study were inactivated at 56°C. for 30 minutes and absorbed with 1/10 volume of washed packed human Group O erythrocytes. Human leptospirosis sera were collected in Yugoslavia. Human sera were inactivated at 56°C. for 30 minutes before use.

Erythrocytes. Human Group O erythrocytes from 3 donors were used exclusively in this study. The erythrocytes were stored in Alsever's solution at 0° to 4°C., and were used within 2 weeks. On the day of a test, the erythrocytes were washed 3 times in isotonic phosphate saline solution (NaCl, 6.8 g.; Na_2HPO_4, 1.05 g.; KH_2PO_4, 0.81 g.; distilled water, 1,000 ml.; pH, 6.8).

Preparation of the leptospiral-ESS. 0.5 g. pure sodium taurocholate (Pfanstiel Chemical Co., Waukegan, Ill.) was dissolved in 10 ml. of the leptospira suspension which was kept at 37°C. for 2 hours and than at 0° to 4°C. for 16 to 20 hours. 90 ml. of absolute alcohol were then added. The alcohol-bile salt-leptospira combination was mixed thoroughly and kept for two hours to allow for complete flocculation. The alcohol precipitation step must be carried out at 0° to 4°C. The precipitate was collected by centrifugation at 1,500 r.p.m. for 5 minutes and resuspended in 10 ml. of isotonic phosphate saline solution containing merthiolate, 1:5,000. The resulting faintly turbid solution constituted the leptospiral-ESS preparation. This procedure is referred to as the bile salt-alcohol method.

Titration of the ESS. Serial 2-fold dilutions of the ESS preparation were made in isotonic phosphate saline solution. To 1 ml. of the diluted ESS, 0.1 ml. of 10% human group O erythrocytes was added. The ESS-erthrocyte mixture was kept in a 37°C. water bath for 1 hour. The erythrocytes were kept dispersed in the diluted ESS by shaking the mixture every 15 minutes. The sensitized erythrocytes were washed twice with isotonic phosphate saline solution by centrifugation at 1,500 r.p.m. for 5 minutes and resuspended in 1 ml. of the same diluent. 0.1 ml. of the sensitized erythrocytes were added to 0.4 ml. of a known positive serum, diluted to 4 times its ESS antibody titer. After shaking, the tubes were kept in a 30°C. water bath for 16 to 20 hours. Agglutination was indicated by macroscopic clumps of erythrocytes upon gentle shaking of the tubes. The highest dilution of the preparation which sensitized the erythrocytes under these experimental conditions was considered one unit of ESS. When one batch of ESS is titrated at different times by this method, the endpoint may vary as much as, but not more than, 4-fold.

The leptospiral-ESS test. Sensitized erythrocytes were prepared by mixing 1 part of 10% erythrocytes with 10 parts of diluted ESS containing at least 4 units of ESS per ml. The mixture was incubated and the erythrocytes were washed and resuspended as described in the previous paragraph. Serial 2-fold dilutions were made of the test sera. To 0.4 ml. of diluted serum, 0.1 ml. of 1% sensitized erythrocytes was added. The tubes were shaken and kept in a 30°C. water bath for 16 to 20 hours. Agglutination was indicated by clumps of erythrocytes upon gentle shaking of the tubes. By this method, the antibody titers of several known positive sera were reproducible within a 4-fold difference. The presence of antibodies against human erythrocytes not treated with ESS must be detected by testing the serum with 1% washed erythrocytes; when present, such antibodies were removed by absorption prior to the ESS test.

RESULTS

Factors affecting the concentration of ESS. In the early phase of this work, when leptospirae were regularly concentrated 10-fold, it was observed that the yield of ESS varied greatly. Experiments were then carried out to determine factors responsible for such variation. In order to eliminate the leptospira concentration factor, all leptospiral suspensions were adjusted to the same optical density as described in a previous section. Table 1 shows the concentration of ESS obtained from various leptospiral suspensions. The range from 32 to 128 units per ml., a 4-fold difference, is attributable to the inherent errors of ESS titrations.

The influence of the age of the leptospiral cultures on ESS content was studied by harvesting *L. can.* and *L. ictero.* cultures on the 7th, 13th and 19th days. The ESS concentrations were respectively 128, 128 and 32 for *L. can.* and 64, 128 and 128 for *L. ictero.*; the differences were within the expected variation of the method.

L. can. and *L. ictero.* grown in the media described by Stuart (1946), Chang (1947) and Korthof (1928) also did not vary significantly in the yield of ESS. The values were 128 and 128 for *L. can.* and 128, 64 and 160 for *L. ictero.*

Methods of disintegrating the leptospirae were also studied. One suspension of *L. can.* was subjected to sonic vibration for 10 minutes; no leptospirae were seen in darkfield preparations after such treatment. The sonic vibrated *L. can.* suspension, however, contained only 4 units of ESS in contrast to 128 units by the bile salt-alcohol method. Suspensions of *L. ictero.*, *L. pom.* and *L. aut.* were sub-

TABLE 1

Concentration of leptospiral-ESS in various preparations

ESS PREPARATION	UNITS/ML.
L. con	128*
L. ictero	64
L. pom	32
L. heb	128
L. aut	64

* Reciprocals of dilution of ESS preparation giving complete sensitization of 0.1 ml. of 10% erythrocytes.

TABLE 2

Antibody titers of rabbit anti-leptospira sera in leptospiral-ESS and agglutination-lysis tests

RABBIT	IMMUNIZED WITH		ANTIBODY TITERS									
			Leptospiral-ESS test					Agglutination-lysis test				
			L. can.	*L. ictero.*	*L. pom.*	*L. heb.*	*L. aut.*	*L. can.*	*L. ictero.*	*L. pom.*	*L. heb.*	*L. aut.*
A	*L. can.*	pre	0*	0	0	0	0	0	0	0	0	0
		post	80	80	160	160	80	6250	0	0	0	0
B	*L. ictero.*	pre	0	0	0	0	0	0	0	0	0	0
		post	160	160	160	320	160	250	31250†	50	0	250
C	*L. pom.*	pre	0	0	0	0	0	0	0	0	0	0
		post	160	160	160	160	80	250	31250†	31250†	0	10
D	*L. heb.*	pre	0	0	0	0	0	0	0	0	0	0
		post	320	320	320	160	320	10	0	0	31250†	0
E	*L. aut.*	pre	0	0	0	0	0	0	0	0	0	0
		post	160	160	160	160	160	0	1250	250	0	31250†

* Negative at 1/10.

† No endpoint.

jected to 20 cycles of freezing and thawing; after such treatment, a faintly turbid supernatant and some sediment consisting of clumps of leptospirae resulted. No ESS were detected. When the same frozen and thawed leptospiral suspensions were treated with 9 volumes of absolute alcohol for 2 hours at 0° to 4°C., the alcohol precipitate contained as much ESS as the preparation obtained by the bile salt-alcohol method.

Factors affecting the leptospiral-ESS test. Certain factors of practical importance that may affect the results of the ESS test were studied. The pH of the diluent, within the range studied (6.5 to 7.5) did not affect the test. Human group O erythrocytes from 3 donors, fresh or stored in an equal part of Alsever's solution at 0°–4°C. for 1 and 2 weeks, were equally suitable for the test. Thorough washing of the erythrocytes is important; unwashed erythrocytes were difficult to sensitize. A suspension of sensitized erythrocytes, when stored at 0°–4°C., was satisfactory for use after 24 but not after 48 hours.

The incubation temperature greatly affects the antibody titer of the leptospiral-ESS test, as with the typhus ESS test (Chang, Snyder and Murray, 1953). Known positive and negative human and animal sera were tested at 37°, 30°, 20° and 4°C. simultaneously. The antibody titer was highest at 4° and 20°C., but the number of false positive reactions also increased. The test was very insensitive at 37°C. At 30°C., the test was sufficiently sensitive, and no definitely proven false positives occurred. For this reason, 30°C. was considered the optimal temperature.

The optimal length of incubation at 30°C. was also studied. Tests were read after 2, and 16–20 hours. In general the endpoints were sharper after 16–20 hours than after 2 hours, but the antibody titers did not differ significantly.

Results of serum study. Pre- and post-immunization rabbit sera were tested by

the agglutination-lysis and the leptospiral-ESS tests. The results are shown in Table 2. It is important to emphasize the contrast in the results of the two tests. In the agglutination-lysis tests, the rabbit antisera agglutinated homologous strains at high serum dilutions. Against the heterologous strains, however, the same sera gave low titers or were negative. In the ESS test, each of the 5 antisera agglutinated *L. can.*-ESS, *L. ictero.*-ESS, *L. heb.*-ESS, *L. pom.*-ESS and *L.aut.*-ESS sensitized erythrocytes to approximately the same titer. Thus the ESS test shows genus specificity while the agglutination-lysis test shows serotype specificity.

The specificity of the leptospiral-ESS test is indicated by the fact that sera from 21 rabbits immunized with *Borrelia novyi*, *Treponema pallidum*, *T. pertenue*, the Reiter's spirochetes, the pathogenic rickettsiae, *Mycobacterium* tuberculosis, vaccinia virus and bovine albumin did not contain any antibodies to leptospiral-ESS.

TABLE 3

*Results of leptospiral-ESS and agglutination-lysis tests with sera from human leptospirosis**

PT. #	DAY OF ILLNESS	LEPTOSPIRAL ESS TITER	AGGLUTINATION-LYSIS TITER			
			icterohem.	*pomona*	*autumnalis*	*sejroe*
1	23	640	100	4000	1000	1000
2	19	0†	—	2000	—	1000
3	28	160	500	4000	2000	500
4	18	160	—	2000	—	100
5	20	640	100	100	100	8000
6	13	160	—	1000	—	100
7	11	640	100	—	—	2000
8	6	160	500	2000	2000	500

* Sera and results of agglutination-lysis tests were kindly sent by Dr. I. Zaharija, Center for Leptospirosis, Yugoslavia Academy of Arts and Sciences, Zagreb, Yugoslavia.

† 0 = negative at 1/10.

—No data available.

TABLE 4

Results of leptospiral-ESS tests on sera of normal subjects and patients recovering from diseases other than leptospirosis

DISEASE	NUMBER OF SUBJECTS	
	Tested	Positive
Syphilis	9	0
Tuberculosis	18	1
Poliomyelitis	9	1
Undiagnosed fever	22	0
Scrub typhus	7	0
Rocky Mountain spotted fever	7	0
None (healthy adults)	129	2*

* Both sera agglutinate live *L. icterohemorrhagiae*; one at 1/50, the other at 1/250.

Tables 3 and 4 show the results of the preliminary evaluation of the leptospiral-ESS tests with human sera. In this evaluation, *L. can.*-ESS and *L. ictero.*-ESS were used interchangeably. Of the 8 cases of human leptospirosis tested, 7 agglutinated leptospiral-ESS treated erythrocytes at serum dilutions of 1/160 to 1/640.

There were 4 positive leptospiral-ESS tests among 201 sera collected from 129 healthy individuals, 9 persons with positive Hinton tests, 18 tuberculosis patients, 22 cases of undiagnosed fever, 9 cases of poliomyelitis, 7 cases of Rocky Mountain spotted fever and 7 cases of scrub typhus.

Out of the 4 positives, 2 agglutinated *L. icterohemorrhagiae* at serum dilutions of 1/250 and 1/50 while the remaining 2 did not agglutinate *L. canicola* or *L. icterohemorrhagiae* by the agglutination-lysis technique of Mochtar.

Preliminary chemical study. One batch of *L. can.*-ESS was subjected to a few simple chemical procedures. The concentration of ESS was titrated before and after such chemical treatment. It was found that heating at 100°C. for 15 minutes did not decrease ESS activity. Heating at 100°C. in 0.1 N NaOH, a method for extracting ESS from typhus rickettsiae (Chang, 1953), completely destroyed *L. can.*-ESS. The ESS was not precipitated by 5% trichloracetic acid. *L. can.*-ESS was soluble in 66% alcohol at 0°C.; a trace of ESS activity was detected in the 80% alcohol insoluble fraction, while all ESS activity was recovered in the 90% alcohol precipitate. These observations suggest that *L. can.*-ESS is non-protein.

DISCUSSION

Evidence has been presented showing that erythrocyte-sensitizing substances (ESS) can be isolated from pathogenic leptospirae by dissolving concentrated suspensions of these micro-organisms in 5% sodium taurocholate, followed by precipitating with 9 volumes of cold absolute alcohol. Based upon the study of 5 strains of leptospira and their corresponding antisera, the leptospiral-ESS appear to be genus specific. Preliminary study with sera from human leptospirosis shows that antibodies to leptospiral-ESS were present in 7 out of the 8 sera tested. Only 4 of the 201 non-leptospirosis human sera agglutinated erythrocytes treated with leptospiral-ESS. Two of the 4 were also positive in the agglutination-lysis test using *L. can.* and *L. ictero.* Much more extensive evaluation of the leptospiral-ESS test with known positive human leptospirosis sera would be highly desirable. Since such sera are not available to our laboratory, we offer this report in the hope that other laboratories will work with the test.

SUMMARY

Serologically active erythrocyte-sensitizing substances (ESS) have been isolated from leptospirae. A method is described for the determination of antibodies to leptospiral-ESS. By this method the ESS obtained from each of the five strains studied, *L. canicola*, *L. icterohemorrhagiae*, *L. hebdomadis*, *L. pomona* and *L. autumnalis* reacted identically, which suggests that these leptospiral-ESS are genus, not serotype, specific.

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ADDENDUM

In the interval between the submission of this paper for publication and its acceptance, several important observations were made:

1. ESS were obtained from leptospirae without the use of bile salt. The method consisted of shaking 5 ml. of leptospiral suspension with 5 ml. of absolute ethanol at 0 to 4°C. for about 4 hours. The mixture was centrifuged at 1000 r.p.m. for

10 minutes. The sediment was discarded. To the supernatant fluid 40 ml. of absolute ethanol were added. A small amount of precipitate was formed after 16–24 hours at 0° to 4°C. The precipitate was collected by centrifugation at 1000 r.p.m. for 10 minutes and redissolved in 5 ml. of 0.85% NaCl solution. The ESS concentrations of such preparations were comparable to those obtained by the bile salt-alcohol method.

2. The leptospiral-ESS test was performed on serial serum specimens from 7 proven cases of human leptospiral infection. The sera and the results of the agglutination-lysis tests were kindly furnished by Col. Robert H. Yager of the Veterinary Division, Army Medical Service Graduate School, and the results are made available with his permission. The strain of leptospirae causing the illness in each case had previously been identified by the agglutination-lysis test. An ESS preparation derived from *L. canicola* was used in this evaluation. The results are shown in Table 5. It was evident that the ESS test was positive in all seven cases. It became positive as early as or earlier than the agglutination-lysis test in the course of infection. The genus specificity of the leptospiral-ESS test was again demonstrated. These results substantiate the potential usefulness of the ESS test in the diagnosis of leptospirosis.

TABLE 5

Antibody titers of 7 cases of human leptospirosis by the agglutination-lysis and the leptospiral-ESS tests

PT.	STRAIN CAUSING INFECTION	DAY AFTER ONSET OF ILLNESS	ANTIBODY TITER	
			Aggl-lysis[a]	ESS[b]
A	*L. ictero* Wijnberg	7	neg.	1280*
		8	100	1280*
		14	1600	1280*
B	*L. bataviae* group	4	neg.	neg.
		7	100	320
		10	6400	1280*
C	*L. bataviae* group	6	neg.	neg.
		38	1600	1280*
D	*L. autumnalis* Fort Bragg	early	neg.	neg.
		late	1600	40
E	*L. hebdomadis* group	5	neg.	neg.
		13	400	1280*
F	*L. hebdomadis* group	4	neg.	1280*
		16	6400	1280*
G	*L. pyrogenes*	2	neg.	neg.
		36	1600	320

[a] The agglutination-lysis tests were performed in the laboratory of the Veterinary Division, Army Medical Service Graduate School. Only the titers against the homologous serotype of leptospira were reported. Lowest dilution of serum used in the test was 1 to 100.

[b] The ESS preparation was obtained from *L. can.* Lowest dilution of serum used in the ESS test was 1 to 10.

* Endpoint not reached.

3. Preparations of leptospiral-ESS are stable for relatively short periods. While rickettsial-ESS remained stable for at least one year (Chang, Snyder and Murray, 1954) the leptospiral-ESS prepared by the bile salt-alcohol method was apparently not as stable. One batch of ESS from *L. heb.* lost all its activity within one week at 0° to 4°C. Another preparation from the same strain showed the same ESS activity after one month and one-fourth its original ESS activity after 3 months at 0° to 4°C. Two batches of *L. ictero.*-ESS were fully active for 6 weeks but in 3 months had lost about three-fourths of their potency. All eight batches of ESS prepared from *L. ictero.*, *L. can.*, *L. pom.*, *L. heb.*, and *L. aut.* retained only one-fourth to one-sixteenth of their original ESS activity after storing for 3 months at 0° to 4°C. Methods of preserving ESS activity are being studied in this Laboratory.

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The authors also wish to thank Col. Robert H. Yager for making some of his collection of human leptospirosis sera available for the evaluation of the leptospiral-ESS test.

COMPLEMENT FIXATION TEST WITH A TRIPLE ANTIGEN FOR SYPHILIS, TUBERCULOSIS, LEPROSY OR CHAGAS' DISEASE IN BLOOD BANKS[1]

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Serological tests have been used in blood banks for ruling out syphilitic donors. In South American countries, where leprosy and American trypanosomiasis (Chagas' disease) are endemic and the incidence rates for tuberculosis are high, the serological examination for syphilis alone is not sufficient. The transmission of Chagas' disease through blood transfusion has been demonstrated by Freitas *et al.* (1952). Attention was called to leprous donors after an accidental observation. The complement fixation test with an extract of tubercle bacilli was positive in a patient who some days prior had been used as donor in a blood bank. The diagnosis of leprosy in this patient was confirmed by the demonstration of typical acid-fast bacilli in a cutaneous lesion.

This problem is presented when volunteers coming from places where leprosy and American trypanosomiasis are endemic are used in blood banks instead of well controlled professional donors. Therefore, a screen test for serological exclusion of syphilis, leprosy, tuberculosis and Chagas' disease would appear highly desirable.

Results of the complement fixation test with triple antigen applied to 786 donors in a blood bank in the City of São Paulo (Brazil) are presented in this paper.

PRINCIPLES, MATERIAL AND METHOD

Principles. The principles governing this test are the specificity and independence of the antigen-antibody reactions in the presence of other antigens or antibodies. Each specific antigen-antibody complex reacts with complement as if the other components were absent. It is well known that in *Salmonella* typing by the Kauffmann-White technique, complex antigens react specifically with the corresponding antibodies, independently of the presence of other antigens.

Material. 1. *Sera.* Sera from patients with syphilis, leprosy or Chagas' disease were tested by complement fixation employing cardiolipin antigen, tubercle bacillus and *Trypanosoma cruzi* extracts. Those reacting only with the corresponding antigen were selected. Portions of these sera were used for preparing a pool of reacting sera.

Sera from blood donors were tested with the triple antigen and with each one of the antigens, in complement fixation tests.

[1] A preliminary report on this subject was presented to the "Departamento de Patologia da Associação Paulista de Medicina" on September 16, 1952.

2. *Antigens.* Cardiolipin antigen No. 72 was employed as recommended by Maltaner and Maltaner (1945) in maximally reactive doses for the detection of syphilis. *Trypanosoma cruzi* extract was prepared from cultures according to the technique developed by Freitas and Almeida (1949). *M. tuberculosis extract*, according to Maltaner and Maltaner (1948), is an aqueous extract of tubercle bacilli previously treated with acetone; this antigen reacts with tuberculous and leprous sera (1940). The triple antigen is a mixture of the three previously described antigens in dilutions adjusted for optimal proportions of each one of them. Each antigen was diluted with one-third of the volume of saline required for its dilution when employed alone. When the three dilutions of antigens are mixed for preparing the triple antigen, each one of them is diluted to provide the optimal dose.

Method. The tests were performed basically according to the technique of Wadsworth, Maltaner and Maltaner (1938) which can be summarized as follows: the total volume used in the test is 0.5 ml. Complement is titrated against a 5% standardized suspension of sheep cells maximally sensitized with an equal volume of amboceptor. The unit of complement is the amount required for 50% hemolysis. Patient's serum is used in an amount of 0.05 ml. either undiluted or diluted in pooled nonreacting serum. The pooled reacting serum is used in an amount of 0.15 ml. either undiluted or diluted. The terms *reacting* and *nonreacting* sera as used in this paper refer to sera that did or did not fix complement with the antigen used in the complement fixation test. Antigen and complement are so adjusted as to detect the maximal reaction obtainable with each quantity of reacting serum tested. In the test 3, 6, 9 and 12 units of complement are used. The doses of antigen used with 6, 9 and 12 units of complement are respectively two, three and four times as great as that used with 3 units. In the test with the triple antigen, 3 units of complement were employed. The reactivity of the serum and antigen alone is tested with 1 and 2 units of complement.

The time and temperature allowed for fixation varied with the different systems: four hours in the refrigerator (3°C.–6°C.) in the test for syphilis, but one and one-half hours in the water-bath at 37°C. for tuberculosis, leprosy, Chagas' disease and for the triple antigen. Sensitized cells are added in amounts of 0.2 ml., allowing fifteen minutes in the water-bath at 37°C. for hemolysis.

All reactions are read with the aid of a photo-electric colorimeter in the supernatant fluids after adding 0.5 ml. of cold saline and centrifuging at 1,500 r.p.m. for 5 minutes (Almeida, 1950). They are evaluated in terms of the relative amounts of complement required for 50% hemolysis under the different conditions of the test, that is, in the presence of serum or antigen alone or in combination. The relative amounts of complement required for 50% hemolysis, as indicated by the degree of hemolysis obtained with a given amount of complement, can be calculated by means of conversion factors derived from titrations of complement in the presence of the different reagents of the test, for each one of the systems (tuberculosis-leprosy, syphilis and Chagas' disease). Thus the relative amounts of complement required, under given conditions, to give 50% hemolysis, can be read from previously prepared charts and the titers can be

easily calculated as the ratio between the number of units of complement required for 50% hemolysis with serum and antigen and the number of units of complement required for 50% hemolysis with serum alone.

RESULTS

1. Reacting sera from patients with syphilis, leprosy or Chagas' disease were tested against the corresponding antigens and with the triple antigen. The titers of these sera with the triple antigen were very close to those determined with each one of the specific antigens (Table 1).

When sera from Chagas' disease were tested with the triple antigen, sometimes the titers were higher than those determined with *T. cruzi* antigen. This difference in titers suggests some degree of cross reaction between *T. cruzi* antibody and tubercle bacillus antigen. We have observed this same type of cross reaction with some sera of Chagas' disease when tested with tubercle bacillus extract. On the other hand, leprous sera do not react with our *T. cruzi* antigen.

2. The pool of reacting sera was tested with cardiolipin antigen, tubercle bacillus extract and *T. cruzi* antigen. The titers obtained were close to those of each serum with its specific antigen (Table 1).

3. A total of 786 sera from blood donors were tested with the triple antigen and at the same time with each one of the three different antigens. The results are presented in Table 2.

It should be noticed that none of the sera that did not react with the triple antigen showed any reaction in the tests for tuberculosis-leprosy, syphilis or Chagas' disease, indicating that no false negatives occurred when the test was carried out with the triple antigen. Every serum which reacted with any of the specific antigens, also reacted with the triple antigen.

On other hand, 76 sera which reacted with the triple antigen, did not show any reaction in the specific tests. These results could be due to the cumulative effects

TABLE 1

*Example of the independence of complement fixation tests when performed in the presence of the triple antigen or in the presence of different antibodies**

SERUM POOL FROM	SERUM TESTED	ANTIGEN USED IN C.F. TEST	TITER OF THE SERUM
Syphilis	Alone	Cardiolipin 72	19.6
	Alone	Triple-antigen	18.0
	Pooled†	Cardiolipin 72	21.0
Leprosy	Alone	Tb-extract	33.0
	Alone	Triple-antigen	27.0
	Pooled	Tb-extract	31.0
Chagas' disease	Alone	*T. cruzi* extract	6.0
	Alone	Triple antigen	9.0
	Pooled	*T. cruzi* extract	5.8

* In this comparative series the preliminary incubation was 90 minutes at 37°C. in water-bath.

† Mixture of the three serum pools.

TABLE 2

Results of complement fixation tests in 786 blood donors

TRIPLE ANTIGEN	ANTIGEN			TOTAL
	TB-extract	Cardiolipin	*T. Cruzi* extract	
No reaction	−	−	−	599
Reaction (183 sera)	−	−	−	76*
	+	−	−	27
	−	+	−	36
	−	−	+	31
	+	+	−	2
	+	−	+	8
	−	+	+	3
Anticomplementary sera				4

* Reacted to triple antigen but not to individual antigens.

of the three antigens upon the complement. When three units of complement are used with the triple antigen, the anticomplementary action of the antigen may be added to the effect of some sera upon complement, and less than 90 % hemolysis occurs. The test is recorded as "*reaction*". However, when these sera were tested with each antigen, hemolysis higher than 90 % occurred in every test, and was read as "*no reaction*". Since the test with triple antigen was devised for the screening of nonacceptable blood donors, it has fulfilled the necessary requirements by excluding the patients with reacting sera.

This type of test could be used whenever a screening test is required, as for instance, in military medicine or in public health laboratories. If a serological diagnosis is required, the reacting sera should be submitted to complement fixation tests with each one of the specific antigens.

SUMMARY

A quantitative complement fixation test using a triple antigen, made up of cardiolipin No. 72 for syphilis, *T. cruzi* extract for Chagas' disease and a tubercle bacillus extract for tuberculosis and leprosy, is presented. Experimental work has been done to establish the basic principles governing the reaction by demonstrating that the specific systems react independently of the presence of other antigens.

Sera from 786 blood donors were tested against the triple antigen and against each one of the specific antigens, in complement fixation tests. The 599 sera that did not react with the triple antigen did not show any reactivity with the antigens for syphilis, tuberculosis-leprosy or Chagas' disease; no false negatives occurred with the triple antigen. The 103 sera which reacted with any one of the specific antigens, reacted also with the triple antigen. Four sera were anticomplementary, simulating "reaction" with the triple antigen; 76 sera gave "reaction" with the triple antigen but did not show any specific reaction in the tests for syphilis, Chagas' disease, tuberculosis or leprosy. These results could

be due to the cumulative anticomplementary effect of these sera plus that of the antigens composing the triple antigen.

The preceding results indicate that a screen test employing the triple antigen should be used instead of the regular test for syphilis, in areas where syphilis, tuberculosis, leprosy, and Chagas' disease are endemic.

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ANTHELMINTIC TREATMENT OF UNCINARIASIS[1]

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For a long time it has been generally agreed that the best anthelmintic treatment in hookworm disease is tetrachlorethylene, U.S.P., followed by a cathartic of sodium sulfate or magnesium sulfate. But anyone who has administered this combination of drugs to a number of patients will have been concerned at the nausea, vomiting, shock, and sometimes even collapse that not infrequently follow this treatment. These untoward symptoms occur with greatest frequency and in most marked degree in cases of severe hookworm disease where the patient is already weakened by the anemia resulting from the infection. In very severe cases, having perhaps 2.0 gm. or even 1.5 gm. of hemoglobin per 100 cc. of blood, the authors have sometimes feared to give the tetrachlorethylene-sodium sulfate treatment because of the shock it provokes. In some of these cases we have postponed the anthelmintic treatment, trying meanwhile, with diet, iron and bed rest, to improve the condition of the patient to the point where he may be given the deparasitizing treatment. But this attempt is not always successful and everyone who has given numerous hookworm treatments in an area where the disease occurs in severe form—any warm climate, that is, which has as much as 60 inches of average annual rainfall—will have had cases that have died from the effects of the disease before the parasites could be removed.

Tetrachlorethylene without purgative. During the past five years, we have had occasion to treat large numbers of cases of hookworm disease, many of them severe. Nearly all of these have received tetrachlorethylene and, until a while ago, a purge of sodium sulfate was administered 20 to 30 minutes afterward. In the course of this experience we came to think that perhaps the use of a cathartic less drastic than the sodium sulfate might help to avoid the undesirable reaction after the treatment; attention was devoted to the possibility of employing compound jalap powder or extract of cascara sagrada instead of the saline purge, but this came to nothing.

We then administered a few treatments consisting of very small doses of tetrachlorethylene without any purge at all. The patients experienced none of the disturbing post-treatment symptoms mentioned above. The dosage of tetrachlorethylene, administered without purge, was then raised to 3.0 cc. for adults with proportionately smaller doses for children, the same dosage we had been using previously with the saline purge. Since March 1, 1952, we have administered more than 591,000 hookworm treatments consisting of tetrachlorethylene

[1] The studies and observations upon which this paper is based were done by the Hookworm Control Division of the Secretariat of Public Health of the Dominican Republic, with the cooperation of the Division of Medicine and Public Health of The Rockefeller Foundation.

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without purge, to about 385,000 persons. The absence of post-treatment symptoms in these cases has been notable, even from larger doses of tetrachlorethylene than we had ever given when using the saline purge. Occasionally a patient will feel a little giddy or drowsy, but that is all. Children five years of age and over stand the purgeless treatment as easily as adults. We can treat a thousand patients or more in a morning in one of our clinics, and not one will even have to lie down after taking the anthelmintic. When we used to give the saline purge, we could treat only a fifth of that number in a day; there was so much sickness that we had to have facilities for individual, emergency attention. Furthermore, patients that have hookworm disease in a very severe degree—perhaps with 1.5 gm. of hemoglobin per 100 cc. of blood, massive edema, and cardiac failure—can take a full dose of tetrachlorethylene without a purge and show no unfavorable reaction from the treatment. We have been able to save many of these extremely severe cases with the purgeless treatment, where previously we would not have dared give the anthelmintic with the purge.

Pharmacology of tetrachlorethylene. Lamson *et al.* (1929) made an extensive investigation of the pharmacology of tetrachlorethylene. They found that tetrachlorethylene is not readily absorbed from the intestinal tract of experimental animals. When enormous doses were given to animals of different species, absorption might take place with symptoms and even death, but the authors state that the symptoms were those of an overdose of an hypnotic, not those of chemical changes secondary to liver damage, such as is the case with carbon tetrachloride, the anthelmintic that was replaced by tetrachlorethylene. The same kind of death was caused by inhalation of high concentrations of tetrachlorethylene vapor, but the experiments of these investigators showed no true necrosis of liver or kidney in the experimental animals. This was true even with doses of tetrachlorethylene up to stomach capacity (275 cc.), and after several hours of inhalation. Furthermore, dogs were given doses of 4.0 cc. per kilo of body weight, at intervals of two or three days for periods of several months, without producing any pathological changes in the liver. The fact that tetrachlorethylene is apparently unabsorbed from the intestinal tract could account for the absence of pathological changes after administration of the drug, but Lamson *et al.* add that it is very striking to find that no changes occur in laboratory animals, even after prolonged inhalation of this substance.

Posology of tetrachlorethylene and anthelmintic efficiency. Every author we know recommends 3.0 cc. of tetrachlorethylene as the adult dose, with proportionate dosage for children; in all cases a saline purge after the drug is stated to be necessary. This is the dosage we were using before we omitted the saline purge. As soon as we began to give the tetrachlorethylene without the purge, we found that we could safely increase the dosage. As would be expected, the increase in dosage resulted in increased anthelmintic efficacy. Of the more than 591,000 treatments reported above, 388,623 were given with a dosage scale of 4.0 cc tetrachlorethylene for adults with proportionate doses for children. Since August 1, 1953, we have been using a dosage scale of 5.0 cc. for adults and proportionate doses for children. To date we have administered 52,611 treatments with the 5.0

cc. scale of dosage, and there are no more untoward symptoms than with the smaller dosage.

We have tested the anthelmintic efficiency of several different dosages by collecting and counting the hookworms expelled after the treatment. We have a small pavilion ward with five beds, and an adjoining bedroom accommodates an employee who is on duty 24 hours a day. The patients are under absolute control and the hookworm collections from each are complete. When the test cases are completely controlled, the number of cases does not have to be as large in order to have validity as it does when the test treatments are given under field conditions where control of the patients is not possible. In the test treatments, the anthelmintic is given in the morning with the patient having fasted since the previous evening. Each patient is given repeated treatments, usually at four-day intervals, until a microscopic fecal examination by the Willis salt flotation, concentration method is negative for hookworm eggs.

We tested the efficacy of the 3.0 cc. dose, followed by the saline purge, in five cases in adults. Table 1, cases 1 to 5 inclusive, shows the results obtained. In none of the five cases were we able to remove all the hookworms with the purge treatment. Four of these cases received five treatments apiece with purge, and one received six treatments with purge. It appeared undesirable, because of the patients' condition, to give these five cases any more treatments with purge and so, in each case, further treatments consisted of 5.0 cc. tetrachlorethylene without purge. In cases 1 to 5 in Table 1, note the low percentage of hookworms removed by each of the 3.0 cc. doses with purge. This treatment then, the treatment that we formerly used and the one recommended by various authors, is not very efficient in removing the hookworms.

In the same Table 1, cases 6 to 11 inclusive are adults and children that received about the same dosage as cases 1 to 5; that is, 3.0 cc. for adults and proportional dosage for children and for adults of less than 120 pounds body weight. Cases 6 to 11, however, received no purge. The increase in anthelmintic efficiency is very evident.

When we found that the tetrachlorethylene without purge caused so little trouble, we increased the dose to 4.0 cc. tetrachlorethylene for adults. In regard to the dosage for children, we decided after considerable testing to base this upon body weight rather than upon age of the child. The advantages of this are obvious. The only disadvantage is that the patient has to be weighed. But this has been our standard clinical practice, together with a microscopic fecal examination and a blood hemoglobin determination for each patient. When any one of our clinics can administer treatment to more than a thousand persons in a morning, it is clear that the necessity of weighing the patients is not a very serious handicap. We therefore adopted the dosage scale of 0.05 cc. tetrachlorethylene per pound of body weight, with a maximum dose of 4.0 cc.

We have 21 hookworm-counted cases that received the tetrachlorethylene dose at rates varying from 0.03 to 0.06 cc. per pound of body weight, with a maximum dose of 4.0 cc. The average dose of those that received less than 4.0 cc. was about 0.05 cc. per pound of body weight. None of the 21 cases received the purge.

TABLE 1

Comparative anthelmintic efficiency of tetrachlorethylene with and without a saline purge

CASE NUMBER	AGE IN YEARS	WEIGHT IN POUNDS	HEB. IN GRAMS	NUMBER OF TREATMENT	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED	NUMBER OF TREATMENT	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED	NUMBER OF TREATMENT	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED	NUMBER OF TREATMENT	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED
1	26	110	4.8	1st	3.0(P)*	1569	417	26	2nd	3.0(P)	1152	405	35	3rd	3.0(P)	747	130	17	4th	3.0(P)	617	139	22
				5th	3.0(P)	478	228	48	6th	5.0†	250	227	91	7th	5.0	23	23	100					
2	23	116	6.4	1st	3.0(P)	309	61	20	2nd	3.0(P)	248	97	39	3rd	3.0(P)	151	29	19	4th	3.0(P)	122	94	77
				5th	3.0(P)	28	26	93	6th	5.0	2	2	100										
3	26	120	4.8	1st	3.0(P)	889	553	62	2nd	3.0(P)	336	242	72	3rd	3.0(P)	94	45	48	4th	3.0(P)	49	11	22
				5th	3.0(P)	38	29	76	6th	5.0	9	9	100										
4	30	111	4.3	1st	3.0(P)	1322	333	25	2nd	3.0(P)	989	340	34	3rd	3.0(P)	649	150	23	4th	3.0(P)	499	76	15
				5th	3.0(P)	423	172	41	6th	5.0	251	245	98	7th	5.0	6	6	100					
5	33	120	4.8	1st	3.0(P)	1197	686	58	2nd	3.0(P)	504	130	26	3rd	3.0(P)	374	85	23	4th	3.0(P)	289	14	5
				5th	3.0(P)	275	92	33	6th	3.0(P)	183	13	7	7th	5.0	170	152	89	8th	5.0	18	18	100
6	18	108	3.4	1st	2.7	3063	2820	92	2nd	2.7	243	228	94	3rd	2.7	15	14	93	4th	2.7	1	1	100
7	28	112	4.8	1st	3.0	2636	1947	74	2nd	3.0	689	484	70	3rd	3.0	205	183	89	4th	3.0	22	22	100
8	45	114	4.8	1st	2.8	1087	825	78	2nd	2.8	233	152	65	3rd	2.8	81	68	84	4th	2.8	13	13	100
9	9	45	4.3	1st	1.2	1008	928	92	2nd	1.2	80	68	85	3rd	1.2	12	12	100					
10	17	113	8.8	1st	3.2	1578	1413	90	2nd	3.2	165	146	88	3rd	3.2	19	19	100					
11	18	101	4.8	1st	2.9	2226	1067	48	2nd	2.9	1159	892	77	3rd	2.9	267	165	62	4th	2.9	102	81	79
				5th	2.9	21	16	76	6th	2.9	5	5	100										

* 3.0(P) means 3.0 cc. tetrachlorethylene, followed in 20 to 30 minutes by 30 gm. sodium sulfate.

† 5.0 means 5.0 cc. tetrachlorethylene without cathartic.

TABLE 2

Test treatments

4.0 cc. tetrachlorethylene maximum dose

CASE NUMBER	AGE IN YEARS	WEIGHT IN POUNDS	HEM. IN GRAMS	1st treatment				2nd treatment				3rd treatment				4th treatment				5th treatment			
				DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED
12	29	108	1.9	3.2*	1159	1030	89	3.2	129	109	84	3.2	20	20	100								
13	8	40		1.2	447	444	99	1.2	3	3	100												
14	12	63	8.0	2.0	1296	1276	98	2.0	20	20	100												
15	13	68		2.2	629	596	95	2.2	33	33	100												
16	14	82	9.1	2.7	688	609	89	2.7	79	79	100												
17	30	111	1.9	3.6	5524	5337	97	3.6	187	182	97	3.6	5	5	100								
18	18	87	4.1	2.8	1886	1851	98	2.8	35	35	100												
19	14	68	9.2	2.2	1888	1846	98	2.2	42	42	100												
20	10	46	3.8	1.5	886	726	82	1.5	160	99	62	1.5	61	58	95	1.5	3	2	67	1.5	1	1	100
21	8	35	4.1	1.4	1344	1205	90	1.4	139	137	99	1.4	2	2	100								
22	14	62	2.9	2.4	1637	1210	74	2.4	427	347	80	2.4	87	78	90	2.4	9	9	100				
23	12	60	5.3	2.4	615	582	95	2.4	33	32	97	2.4	1	1	100								
24	12	54	5.3	2.0	881	690	78	2.0	191	130	68	2.0	61	43	71	2.0	18	18	100				
25	47	122	4.1	4.0	2127	2049	96	4.0	78	78	100												
26	37	155	9.6	4.0	481	445	93	4.0	36	36	100												
27	60	122	1.8	4.0	531	519	98	4.0	12	12	100												
28	9	43	7.6	2.5	63	29	46	2.5	34	7	20	2.5	27	21	78	2.5	6	6	100				
29	11	52	9.6	3.1	639	381	60	3.1	258	202	78	3.1	56	56	100								
30	10	54	7.6	3.2	930	883	95	3.2	47	46	98	3.2	1	1	100								
31	11	58	7.6	3.4	1014	1013	99	3.4	1	1	100												
32	11	58	6.4	3.4	958	552	58	3.4	406	193	47	3.4	213	149	70	3.4	64	59	92	3.4	5	5	100

* 3.2 means 3.2 cc. tetrachlorethylene without cathartic.

TABLE 3

Test treatments

5.0 cc. tetrachlorethylene

CASE NUMBER	AGE IN YEARS	WEIGHT IN POUNDS	HEM. IN GRAMS	1st treatment				2nd treatment				3rd treatment				4th treatment				5th treatment			
				DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED
35	70	100	3.7	5.0*	1308	1308	100																
36	56	132	3.7	5.0	1138	1107	97	5.0	31	31	100												
37	25	140	6.7	5.0	2824	2663	94	5.0	161	159	99	5.0	2	2	100								
38	26	120	3.7	5.0	1390	1358	97	5.0	32	32	100												
39	19	102	4.8	5.0	623	620	99	5.0	3	3	100												
40	26	145	12.8	5.0	360	355	99	5.0	5	5	100												
41	36	130	4.8	5.0	543	523	96	5.0	20	19	95	5.0	1	1	100								
42	45	110	8.8	5.0	1507	1444	96	5.0	63	59	94	5.0	4	4	100								
43	32	112	4.8	5.0	1919	1715	89	5.0	204	185	91	5.0	19	19	100								
44	22	92	6.4	5.0	898	629	70	5.0	269	265	98	5.0	4	4	100								
45	15	84	4.8	5.0	1765	1683	95	5.0	82	77	94	5.0	5	5	100								
46	30	138	8.0	5.0	1001	812	81	5.0	189	188	99	5.0	1	1	100								
47	30	110	4.8	5.0	1594	1393	87	5.0	201	184	91	5.0	17	17	100								
48	14	85	6.4	5.0	1058	1050	99	5.0	8	2	25	5.0	6	6	100								
49	54	140		5.0	1700	1334	78	5.0	366	333	91	5.0	33	16	48	5.0	17	15	88	5.0	2	2	100
50	20	95	8.0	5.0	1050	1041	99	5.0	9	9	100												
51	49	108	7.6	5.0	271	266	98	5.0	5	5	100												
52	27	124	6.7	5.0	210	205	98	5.0	5	5	100												
53	27	120	7.6	5.0	1341	1165	87	5.0	176	176	100												
54	50	135	1.6	5.0	1658	1607	97	5.0	51	51	100												

* 5.0 means 5.0 cc. tetrachlorethylene without cathartic.

TABLE 4

Test treatments

Tetrachlorethylene and hexylresorcinol alternating

CASE NUMBER	AGE IN YEARS	WEIGHT IN POUNDS	HBN. IN GRAMS	1st treatment				2nd treatment				3rd treatment				4th treatment				5th treatment			
				DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED	DOSAGE	HOOKWORMS BEFORE TREATMENT	HOOKWORMS EXPELLED	PER CENT EXPELLED
55	30	122	9.2	4.0(T)*	1470	1301	88	1.0(H)†	169	70	41	4.0(T)	99	66	67	1.0(H)	33	33	100				
56	25	116	8.9	4.0(T)	1442	1126	78	1.0(H)	316	59	19	4.0(T)	257	196	76	1.0(H)	61	30	49	4.0(T)	31	31	100
57	16	65	8.5	2.6(T)	1816	1582	87	1.0(H)	234	178	76	2.6(T)	56	27	48	1.0(H)	29	29	100				
58	18	100	4.8	1.0(H)	3894	2165	53	4.0(T)	1829	1312	72	1.0(H)	517	234	45	4.0(T)	283	272	96	1.0(H)	11	11	100
59	30	117	4.8	1.0(H)	1279	724	57	4.0(T)	555	553	99	1.0(H)	2	2	100								

* 4.0(T) means 4.0 cc. tetrachlorethylene without cathartic.

† 1.0(H) means 1.0 gm. hexylresorcinol.

Table 2, representing cases 12 to 32, shows the results obtained in these treatments. Ten of the 21 cases were deparasitized with two treatments each, and six of the cases with three treatments. Only one of the 21 cases retained as many as 25 hookworms after the third treatment. This dosage scale, then, is rather efficient in removing hookworms.

Cases 35 to 54, shown in Table 3, received 5.0 cc. of tetrachlorethylene without purge. As the figures show, this treatment is quite efficient. One of the twenty cases, with a fairly heavy infection, was deparasitized with one treatment; nine were deparasitized with two treatments each; and only one case retained hookworms after three treatments. We have given 52,611 treatments with the dosage scale of 0.06 cc. tetrachlorethylene per pound of body weight, with a maximum dose of 5.0 cc., and at present we are using this dosage scale in all treatments given in our clinics. Soft gelatin capsules containing tetrachlorethylene are employed. These come in 1.0 cc., 0.5 cc., and 0.2 cc. sizes and are obtainable from the R. P. Scherer Corporation, Detroit 13, Michigan.

Other test treatments. It is sometimes stated (Carr, 1949) that alternating treatments with tetrachlorethylene and hexylresorcinol are more effective than treatments with either of the two drugs exclusively. We tested alternating treatments of the two drugs and the result is shown in Table 4, cases 55 to 59. It is obvious that there is no advantage in the alternating treatments. It is also clear that in these carefully controlled test cases, hexylresorcinol was inferior to tetrachlorethylene in respect to anthelmintic efficiency against hookworm.

Anthelmintics are sometimes given in divided doses, allowing 15- to 30-minute intervals between fractions, with the idea of increasing the efficacy of the drug. We tested this method of administering tetrachlorethylene in seven hookworm-counted cases. These cases received the 0.05 cc. of tetrachlorethylene per pound of body weight, with a 4.0 cc. maximum dose, without purge. Five of the cases received the anthelmintic in four equal portions with one-half hour between portions, and two received the drug in the same manner but with fifteen minutes between portions. No increase in anthelmintic efficiency was noted.

Sometimes authors recommend that a purge be given the evening before the morning when the anthelmintic is to be given. This makes a theoretical appeal, for with the small intestine empty, as it should be after the evening laxative, one would suppose that more of the anthelmintic would reach more of the hookworms and so result in increased efficiency. We treated seven cases, giving to each, the afternoon before the anthelmintic was to be administered, a dose of a laxative (*Veracolate*, Standard Laboratories, Inc.) that in each of the seven cases caused one or more defecations before the tetrachlorethylene was administered. The dose of tetrachlorethylene was 5.0 cc. in each case, and no purge was given after the anthelmintic. No increase in anthelmintic efficiency was apparent in these cases compared with cases that received similar amounts of tetrachlorethylene but without the pretreatment laxative.

CONCLUSIONS

In the anthelmintic treatment of uncinariasis, tetrachlorethylene, U.S.P., should be given in factory-filled, soft gelatin capsules; it should be administered

in the morning with the patient having fasted since the previous evening, and no cathartic should be given after the anthelmintic. The dosage scale may be 0.05 cc. tetrachlorethylene per pound of body weight, with a maximum dose of 4.0 cc., or it may be 0.06 cc. per pound of body weight, with a maximum dose of 5.0 cc. The latter dosage scale occasions no more untoward symptoms than the smaller dose and will probably be found even more efficacious in removing hookworms.

SUMMARY

Tetrachlorethylene, U.S.P., when administered without being followed by a purge, causes less shock to the patient and is more efficacious in removing hookworms than when the anthelmintic is followed by a saline purge.

A dosage scale of 0.05 cc. tetrachlorethylene per pound of body weight, with a maximum dose of 4.0 cc., is quite efficient in removing hookworms and is safe for the patient. A dosage scale of 0.06 cc. tetrachlorethylene per pound of body weight, with a maximum dose of 5.0 cc., is also highly efficacious and causes no more untoward symptoms than does the smaller dosage.

More than 591,000 treatments have been given to about 385,000 patients using tetrachlorethylene without a purge. Of these, 388,623 treatments were of the first dosage scale indicated above, and 52,611 were of the second dosage scale. At present, the latter is being employed exclusively in our hookworm clinics.

In hookworm-counted, controlled treatments there was no increase in anthelmintic efficiency as a result of alternating treatments with tetrachlorethylene and hexylresorcinol. There was no increase in anthelmintic efficiency as a result of administering the tetrachlorethylene in fractionated doses, nor did emptying the intestine by means of a laxative before the anthelmintic treatment increase its efficacy.

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THE EFFICACY OF PIPERAZINE COMPOUNDS AGAINST *SYPHACIA OBVELATA*, A PINWORM OF MICE[1]

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Hewitt and associates (1948) investigated a large group of piperazine compounds for their activity against the cotton rat filariid, *Litomosoides carinii*, which led to the discovery of "Hetrazan" (1-diethylcarbamyl-4-methylpiperazine hydrochloride), an orally administrable filaricide. Mouriquand, Roman and Coisnard (1951) tested the hydrate of piperazine against *Rhabditis macrocerca* in vitro and against *Aspiculuris tetraptera* and *Syphacia obvelata* in vivo and found it to be active against all three helminths. They extended these studies to man, treating a number of *Enterobius*-infected individuals with piperazine hydrate with successful clinical results. Studies by Standen (1953) confirmed the activity of piperazine hydrate against *Aspiculuris* in mice, and White and Standen (1953) found this compound to be as effective in human enterobiasis as gentian violet. We also have treated a number of *Enterobius* infections with piperazine hexahydrate with promising results, and will report these data in a separate publication.

During the past several years we have been evaluating the anthelmintic activity of numerous compounds against the mouse oxyurids, *Syphacia obvelata* and *Aspiculuris tetraptera* (Wells, 1951, 1952 a, b; Chan, 1952). Our studies using the standard human pinworm chemotherapeutic agents against the mouse pinworms indicate a good correlation in their activity against the related human and mouse worms (Hsieh 1952; Brown, Chan and Ferrell, 1954). All of our data suggest that the mouse pinworms are useful in the study of new compounds which may be of value against *Enterobius* in man. This is especially important since *Enterobius* has not been transmitted successfully to an experimental host.

The present study reports the activity of thirty-two piperazine compounds against *Syphacia* in mice. An attempt was made to correlate the chemical structure of these compounds with their activity. The investigation of additional piperazine compounds is continuing and we are presenting the results of our study to date without implying that the most active anthelmintic member of this group has been found.

MATERIALS AND METHODS

Thirty-two piperazine compounds, including the commercially available Hetrazan, were tested against *S. obvelata*. The procedures used for evaluating the activity of the compounds against *Syphacia* were essentially those described by

[1] The piperazine compounds used in this study, except "Hetrazan," were supplied by The Burroughs Wellcome Company, U. S. A. We also wish to acknowledge their financial support of this project. Miss Sydell Kopilof rendered valuable technical assistance in this study.

Chan (1952) and consist of a comparison, at autopsy, of the number of *Syphacia* harbored by treated mice with those of untreated control mice. All mice were given experimental infections of approximately the same magnitude and all of the developmental stages of the worm, including adult worms, were therefore exposed to the drug. All variables such as the age of infection, the method of administering the drugs, the number of days of treatment and the time of autopsy were kept uniform to facilitate the comparison of the relative activity of the compounds. The compounds were given by stomach tube, usually in amounts approximately one-third of the oral LD_{50} for mice. Compounds which exhibited activity were given in several dosage regimes in order to ascertain their efficacy in minimum amounts. Because of the relatively standardized experimental infections of *S. obvelata*, six to eight mice were used for one assay; one-half of the animals received treatment and the other half served as controls. Autopsies and worm counts were performed two days after the cessation of chemotherapy. Tests against specific developmental stages of *Syphacia* were done with one compound, piperazine hydrochloride, found promising in the routine studies.

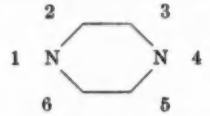
RESULTS AND DISCUSSIONS

The several piperazine compounds varied greatly in their activity against *Syphacia obvelata* (Table 1). A number of the piperazines, when given in massive doses of 1,000 to 3,000 mg. per kg., were effective against the pinworms, but they were relatively ineffective when given in 200 to 300 mg. per kg. doses. Several of these compounds, 50-418A, 52-162, 52-349, 52-369, 52-372, 52-402, 53-94, were toxic to the mice, especially in large dosages; an occasional mouse died of acute toxicity and frequently the mice lost weight. Hetrazan, a piperazine which is active against several microfilariae and *Ascaris lumbricoides*, was not effective against *Syphacia* in doses of 250 mg. per kg. for two days.

The hydrochloride (52-325A, D) and dihydrochloride (52-325) of piperazine and the free base itself (52-325B_1) exhibited the greatest activity against the worms and in doses of 200 mg. per kg. on two successive days reduced the worm burden 73 to 83 per cent. The hydrochloride, when given on two successive days at the rate of 500 mg. per kg., effected a 99 per cent reduction in *Syphacia*. Dead worms were found in the fecal pellets passed by the mice three hours after the drug was administered. All three of these compounds were well tolerated by the mice in the dosage employed, since the LD_{50} dose is 4 grams per kg. as base. Their activity was uniformly greater against the mature worms than against the immature forms. The live worms remaining in the mice post-treatment were usually only the immature, partially developed stages. This observation was confirmed in detail in using piperazine hydrochloride. Groups of mice were infected with *Syphacia* and the treatment administered after the worms had attained various ages. The percentage of worms removed by 200 mg. per kg. of the drug on two consecutive days varied from 100 per cent for mature worms 6–10 days old to only 6 per cent of the worms which were 1–3 days old (Table 2). Our studies on *Syphacia* in mice support the clinical impression of Mouriquand and associates (1951) who report that the gravid *Enterobius* of man appear to be more suscep-

TABLE 1

The effectiveness of piperazines against Syphacia obvelata *in mice*



Piperazine

WRL NO.	SUBSTITUENT OTHER THAN H AT POSITION				SALT*	DOSAGE Mg/kg./ 2 days	AVERAGE WORM BURDEN		
	1	2	4	5			Treated Group	Control Group	% Reduction
52-325 B_1					base b	200	22	143	83
52-325 A, D					.HCl b	500	2	162	99
						200	25	115	80
52-325					.2HCl b	200	39	143	73
52-325 E					bis-phenyl-acetate	1000	6	144	96
						200	46	96	56
52-367	CH_3—				.HCl b	3000	173	187	7
52-369	C_2H_5—				.HCl b	3000	65	148	56
						1000	51	96	47
52-370		CH_3		CH_3	.HCl b	3000	131	148	11
52-371	CH_3—	CH_3		CH_3	.HCl b	3000	137	148	7
52-349	C_2H_5—		C_2H_5		.HCl b	2000	123	186	34
52-372	C_2H_5—	CH_3		CH_3	.HCl b	3000	150	187	20
52-368	CH_3—	CH_3	CH_3	CH_3	.HCl b	3000	185	187	0
50-418A	n-$C_{12}H_{25}$—				.2HCl s	300	79	144	45
51-266	n-$C_{10}H_{21}$—	CH_3		CH_3	.2HCl s	350	131	120	0
51-299	n-$C_{11}H_{23}$—	CH_3		CH_3	.2HCl s	525	98	111	12
51-319	n-$C_{12}H_{25}$—	CH_3		CH_3	.2HCl s	500	101	150	33
46-164†	$HOCH_2CH_2$—				.HCl b	3000	0	187	100
						400	97	134	28
						200	65	185	65

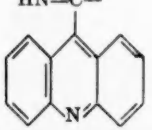
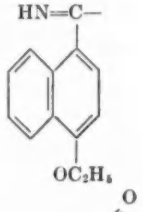
53-94	$HOCH_2CH(CH_3)$—				.HCl s	2000	55	213	74
						500	84	108	22
53-7	$HOCH_2CH_2$—		—CH_2CH_2OH		base b	1250	86	119	28
53-81	$HOCH_2CH(OH)CH_2$—				.2HCl s	1000	86	114	25
52-402	$CH_3C(=O)$—				.HCl s	1200	17	133	87
						200	28	96	71
53-133	$HOOC\text{-}CH(CH_3)$—				base b	2000	67	144	53
52-366	H_5C_2OOC—				.HCl s	160	157	185	16
53-160	H_5C_2OOC—		—CH_2CH_2Cl		.HCl s	70	74	185	60
52-162	H_5C_2OOC—		n-C_8H_{17}		.HCl s	600	73	66	0
52-16	$H_2NC(=O)$—		n-$C_{11}H_{23}$		.HCl s	600	160	120	0
52-9	$H_2NC(=O)$—		n-$C_{16}H_{33}$		.HCl s	1000	120	113	0
53-136	$p\text{-}O_2N\text{-}C_6H_4C(=O)$—		n-C_8H_{17}		.HCl s	300	168	175	4
53-140	$p\text{-}H_2N\text{-}C_6H_4C(=O)$—		n-C_8H_{17}		.HCl s	90	116	144	19
52-67	$H_2N\text{-}C(=NH)$—		n-$C_{16}H_{33}$		.HBr s	500	137	120	0
48-23	$HN{=}C$— 		CH_3		.HCl s	700	143	138	0

TABLE 1—(*Cont.*)

WEL NO.	SUBSTITUENT OTHER THAN H AT POSITION				SALT*	DOSAGE Mg./kg./ 2 days	AVERAGE WORM BURDEN		
	1	2	4	5			Treated Group	Control Group	% Reduction
49-48			CH_3		.HCl s	150	130	138	3
Hetrazan	$(C_2H_5)_2NC(=O)-$		CH_3			250	141	162	13

* b and s indicate that the dosage employed was weighed on the basis of base or salt of the compound.
† LD_{50}, oral, 4 gm./Kg.

TABLE 2

Effect of piperazine hydrochloride (52-325 A or D) against various developmental stages of S. obvelata

DOSAGE	STAGES OF *S. obvelata*	NUMBER OF MICE		AVERAGE WORM BURDEN		
		Treated group	Control group	Treated group	Control group	% reduction
200 mg/kg/2 days	mature worms (6–10 days old)	6	5	0	105	100
200 mg/kg/2 days	all stages (newly hatched to 10 days old)	6	5	24	115	80
200 mg/kg/2 days	immature worms (newly hatched to 5 days old)	4	3	64	144	56
200 mg/kg/2 days	immature worms (newly hatched to 3 days old)	5	5	91	97	6

tible to piperazine hydrate than the immature forms of the worms. It must be remembered, however, that in human pinworm therapy we observe only the worms that are eliminated and have little knowledge of the number or stages of worms that remain. It is possible therefore that, when large numbers of only gravid females are removed by chemotherapy, this is the only stage present.

Since *Enterobius* in man may mature in as short a time as 14–28 days, our studies on *Syphacia* suggest that an interrupted course of therapy over a considerable period of time might be more effective than a short concentrated therapeutic regime. Thus the first 7–10 days of treatment would eliminate all of the mature worms present, and the following 7–10 days' rest period would allow time for the young forms to mature, only to be removed by the second 7–10 days of treatment.

The simple piperazine base and its salts appear to be more effective against *Syphacia* than the more complex substituted compounds, which suggests that the anthelmintic activity resides in the piperazine nucleus. Although quantitative data on the absorption and excretion of piperazine are not available, there is evidence that much of it is absorbed and excreted in the urine (Harned *et al.*, 1948). Theoretically, at least, such a substance should not be very effective against pinworms, which live most of their lives in the large intestine and therefore would not come in contact with an absorbable drug in high concentrations. Hence it was believed that the more complex substituted piperazines, due to a decreased absorption by the intestine, would reach the pinworms in higher concentrations. However, if the compounds are not split to free the active piperazine nucleus, or free it only in small amounts, they would be relatively inactive. The ideal piperazine would appear to be one which is not absorbed in the small intestine and which liberates a quantity of piperazine base or salt in the large intestine.

SUMMARY

The activity of thirty-two piperazine compounds has been tested against *Syphacia obvelata* in mice, and several of them exhibited considerable anthelmin-

tic activity. In general, the simple piperazine base and its salts appear to be more effective against *Syphacia* than are the more complex substituted compounds which were studied. Mature stages of the worm are more vulnerable to piperazine than the immature stages.

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THE EFFECT OF *SCHISTOSOMA MANSONI* INFECTIONS ON LIVER FUNCTION IN MICE

I. Amino Acid Oxidase and Ammonia[1]

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The striking degree of liver damage which accompanies *Schistosoma mansoni* infections in mice suggests that interference with normal liver metabolism has an important role in the etiology of the disease. Ohta and Nishizaki (1936) demonstrated in rabbits infected with *S. japonicum* an increased excretion of several nitrogenous compounds in amounts ordinarily associated with liver malfunction, and Nishizaki (1938) showed that the same infection reduces the production of allantoin by rabbit liver minces. Nishizaki (1940) further established a correlation between the occurrence of increased amounts of amino nitrogen in the urine and reduced liver deamination in the liver of rabbits infected with *Clonorchis sinensis*. No studies on the effects of worm infections on other liver functions have been made.

Preliminary studies on mice infected with *S. mansoni* indicated that an investigation of the effects of the disease on various aspects of liver function might provide bases for an increased understanding of the mechanisms by which this important parasite damages its host. An investigation was planned dealing with detoxication mechanisms in the liver and with liver functions associated with protein and carbohydrate metabolism. This paper is a report on the preliminary findings of the studies on the effects of *S. mansoni* infections on certain liver functions associated with protein metabolism.

MATERIALS AND METHODS

Mature male albino mice were infected by tail exposure to *S. mansoni* cercariae according to a method described by Olivier and Stirewalt (1952). In the early studies 250 cercariae were used but the mortality at this level was such that less severe infections (125 cercariae) were used in the later work. No significant difference in the findings reported here resulted from this change. The assays to be described below were made during the sixth and seventh weeks following infection.

In an effort to reduce the variation in the nonprotein amino nitrogen which existed between individual mice in the early experiments, the following procedure was used. Mice to be studied were taken off food the day before the experiment. On the morning of the experiment one-half of the noninfected controls and one-half of the infected animals were given saline by stomach tube, proportional in

[1] This study was sponsored by the Army Medical Service Graduate School, and was supported (in part) by the Medical Research and Development Board, Office of the Surgeon General, U. S. Army, Washington, D. C.

amount to 0.5 ml. to a 25 gram mouse. The other half of each group was given in a similar manner a 10% solution of tryptic casein digest (Trypticase). After 60 minutes the mice were weighed, killed, and the entire liver removed and weighed. Portions of the liver were taken for dry weight measurements, free amino nitrogen determinations, and oxygen uptake and ammonia measurements. In the early experiments samples of muscle tissue and plasma were also assayed for free amino nitrogen.

The free amino nitrogen was determined by a photometric procedure improved by Frame, Russell and Wilhelmi (1943) and Russell (1944). A modification in the preparation of the tissues from that previously used was made as a means of increasing the accuracy of the determinations. The muscle and liver tissues were homogenized in ground glass homogenizers and diluted to a 5 per cent concentration with water. A 0.2 ml. aliquot of the homogenate was treated with 0.2 ml. of 0.66 N H_2SO_4 and 4 ml. of water and 0.2 ml. of 10% sodium tungstate were added to precipitate the proteins. Following a 60 minute wait the mixture was centrifuged and 2 ml. of the supernatant fluid were used for the amino nitrogen determinations.

The oxygen uptake studies on liver tissue were made on minces. These were prepared by chopping and mashing the liver tissue with the blade of a scalpel on the bottom of an iced Petri dish. A portion of this mince was quickly but accurately weighed and transferred to a Warburg reaction vessel standing in crushed ice. The vessel contained a reaction medium composed of 1.5 ml. of Tyrode solution without the bicarbonate or phosphate, 1.0 ml. of a 0.15 M phosphate buffer at a pH of 7.4, 0.5 ml. of a 0.1 M L-alanine solution and the center well contained 0.1 ml. of a 10% NaOH solution. A duplicate vessel was prepared for each case with the alanine replaced by buffer. The difference in oxygen uptake of the mince on the two media was assumed to be due to the action of the amino acid oxidase system on the alanine (Cagan *et al.*, 1950). Incubation in the water bath was allowed to proceed for 60 minutes at 38°C at which time a final reading was made. The contents of the flask were filtered and a 0.1 ml. aliquot of the filtrate was assayed for ammonia by an adaptation of the Conway micro-diffusion method (Hawk *et al.*, 1947) and a spectrometric analysis according to Russell (1944).

RESULTS

The data recorded in Table 1 show that marked changes in the structural relationships of mouse liver accompanied *S. mansoni* infections. An enlargement of the liver in respect to the total animal was consistently noted. In the uninfected animal the per cent liver weight to body weight varied over a narrow range from 4.1 to 5.4 per cent with a mean of 4.78. The infected animals showed not only an increased liver weight to a mean of 7.16 per cent but the range of variation was much greater. This was unquestionably, in part, a result of an inability to control the level of infection. However, this increased range of variation is not restricted to the present studies but is seen in the results of nearly all biochemical investigations that have so far been attempted on schistosome-infected animals. In addition to increasing the total liver weight, the infection

TABLE 1

Relationship of liver to body weight and per cent dry weight of liver in mice infected with S. mansoni. *The figures in the parentheses are the number of animals in the experiment*

ANIMAL GROUP	RANGE	MEAN	STD. ERROR OF MEAN	DIF. IN MEANS	STD. ERROR OF DIF.
Control—liver % body weight (7)	4.1–5.4	4.8	±.20		
Infected—liver % body weight (7)	5.9–10.6	7.2	±.61	2.4	±.64
Control—% dry weight liver (7)	28–31	29.0	±.46		
Infected—% dry weight liver (7)	25–27	26.0	±.26	3	%.53

caused alterations within the liver. The amount of dry material per unit weight was significantly reduced in the livers of infected mice (Table 1). It is not likely that this represents a loss of material substance. On the other hand, it is probable that the fluid content of the liver was increased by the edema accompanying the infection.

The results of the non-protein amino nitrogen determinations are given in Table 2. The results included in the groups which are indicated simply as control and infected liver were from early studies made before the Trypticase and saline feedings were started. Note, however, that no significant difference exists between the results on these controls and on those which were fed saline. Under both conditions, the value of free amino nitrogen was significantly higher in the livers of infected animals than in those of the noninfected controls. Following Trypticase feeding the amino nitrogen level rose sharply in the infected mice but was not affected in the control mice. Several things must be remarked about these results. First, there was considerable variation in the results obtained on any one group of animals, including the controls. In contrast to the variation in total liver weights mentioned above, it is considered that this represents a true indication of the free amino nitrogen level in the mice, since amino standards run with each experiment were found to vary less than 3 per cent. This variation was not unexpected as it was assumed that, in contrast to the protein amino nitrogen, the free amino nitrogen represented mobilized molecules which would be expected to vary with the changing metabolic conditions. It was for this reason that free amino acid nitrogen rather than protein nitrogen was chosen for measurement. It should also be noted that Trypticase feeding of the infected mice caused a pronounced rise in liver amino nitrogen from a mean of 344 mgm. per gram dry weight in the saline-fed mice to a mean of 374 mgm. per gram dry weight in the Trypticase-fed mice. This did not occur in the normal liver.

The free amino nitrogen in the muscle tissue of the mice was not materially affected by the infection (Table 2). However, the determinations on blood plasma indicated that there was a reflection here of the conditions found in the liver in that a rise in amino nitrogen accompanied infection.

TABLE 2

Free amino nitrogen in tissues of mice infected with S. mansoni. *The figures in the parentheses are the number of animals in the experiment*

ANIMAL GROUP	RANGE OF DETERMINATIONS	MEAN	STD. ERROR	DIF. IN MEANS	STD. ERROR OF DIF.
Control liver (6)	287–304*	294	±3.65		
Infected liver (8)	295–371*	330	±8.46	36	±9.1
Control sal. liver (8)	273–333*	297	±6.22		
Inf. sal. liver (8)	315–367*	344	±6.35	47	±8.9
Control Trypt. liver (6)	251–338*	295	±12.38		
Inf. Trypt. liver (8)	325–430*	373	±12.14	78	±14.18
Control muscle (4)	292–300*	298	±2.68		
Infected muscle (4)	292–350*	314	±12.8	16	±13.11
Control plasma (4)	5.98–6.24†	6.08	±.19		
Infected plasma (6)	7.02–7.36†	7.96	±.44	1.88	±.48

* Mgm/gm dry wt.
† Mgm per cent.

The results on amino acid oxidase activity and ammonia elaboration are presented in Table 3. While the minces from infected livers always gave a higher overall oxygen-uptake activity, this increase was not reflected in the activity of the amino acid oxidase systems. Here the indications were toward a reduction in activity. The possible explanation of the increased activity of infected tissue will be presented below. In the control mice a definite trend toward an increased amino acid oxidase activity was encountered following Trypticase feeding. This result was not found when the infected animals were similarly treated.

The total accumulation of ammonia in the media following the incubation of the liver minces is given in Table 3. The considerable increase in ammonia elaboration following Trypticase feeding to uninfected mice demonstrates the ability of the liver tissue to respond to the stimulus provided by the administration of the casein digest. The media collected following incubation of infected liver minces contained more ammonia than the control liver mince media regard-

TABLE 3

Amino acid oxidase activity and ammonia elaboration of mouse liver minces. The figures in parentheses are the number of animals in the experiment

TREATMENT	CONTROL				INFECTED			
	Alanine substrate	Buffer media	Amino acid oxidase	Ammonia elaboration	Alanine substrate	Buffer media	Amino acid oxidase	Ammonia elaboration
Saline fed	856* (6)	804 (4)	52 ± 7.0	253 ± 10.4†	1125 (6)	1086 (4)	39 ± 6.8	604 ± 15.8 (6)
Trypticase fed	998 (6)	932 (4)	66 ± 5.4	636 ± 12.0 (6)	1174 (6)	1144 (4)	30 ± 7.6	649 ± 14.3 (6)

* Microliters of oxygen per gram dry weight per hour.
† Micrograms ammonia nitrogen produced per gram per hour.

less of previous treatment of the animal. Trypticase feeding did not further increase the ammonia.

DISCUSSION

Following a recent study on the histopathology of schistosome infections, Meleney *et al.* (1953) have given a good account of the morphological changes which occur. On the basis of these histological studies the present observations relating to liver size and the fluid content of infected livers take on added meaning. With the tremendous invasion of leucocytes, epithelioid cells and fibroblasts, a situation similar to an inflammation is set up. This condition inevitably involves a local edema. It is quite likely that both the increase in liver weight and the increased water content are the resultant of these two protective mechanisms. This seems particularly true since no evidence of hypertrophy or hyperplasia of liver tissue has been reported. In view of these histological findings it would seem quite plausible that many of the metabolic deficiencies of infected liver tissue that have been reported were more apparent than real since the sample of tissue selected for test would have contained much material not having liver capabilities. In the present study an attempt was made to remove this criticism by expressing the metabolic activities in terms of dry weight of tissue. This obviously does not eliminate all sources of error. However, the error is reduced to such an extent that, with allowances made for the extrahepatic tissue, certain conclusions may be drawn (*cf.* Table 2).

It will be noted that the administration of tryptic casein digest to the uninfected mice did not materially increase the subsequent amino nitrogen determinations. A similar treatment of the infected mice resulted in a significant rise in the level of amino nitrogen in the liver, demonstrating an inability to handle the sudden influx of amino acids in the casein hydrolysate. Unquestionably, the edema and the invasion of the liver by a considerable amount of nonliver tissue affect total liver functions but it should be noted that there has been no real loss of functional liver tissue at this time. Therefore, it seems likely that the differential between saline and Trypticase feeding represents a true functional deficiency on the part of the liver. Whether this is a result of the infection *per se*, or whether it develops subsequent to the histological changes that occur in the liver is not apparent at this time.

The enzyme studies provide additional evidence that a true functional disability is involved. The amino acid oxidase activity is in itself somewhat reduced in the infected mouse liver. It could be argued that this, as mentioned above, results from the inclusion of nonliver tissue in the liver mince of infected mice. However, the important result to come from these experiments is not the level of activity itself, but the fact that the infected liver cannot respond to the stimulus provided by the Trypticase feeding. This is demonstrated both in the oxygen consumption data and in the elaboration of ammonia. The former data is, in itself, not statistically conclusive, but when considered in relation to the ammonia data it becomes obvious that an interference with normal liver function has occurred. A decrease in amino oxidase activity of mouse liver subsequent to

S. mansoni infection would adequately explain (by reduced deamination) the increases that were noted above in the amino nitrogen level both in the liver and in the blood. It seems logical enough to assume that, if liver function is disturbed in this regard, it is probably also affected in other ways, i.e. ammonia pick-up. Although no studies have as yet been made on this part of the problem, the figures for ammonia given in Table 3 suggest that an interference with the ammonia pick-up mechanism is involved. Thus, although ammonia may be formed more slowly due to a reduction in total amino acid oxidase activity, it would tend to accumulate because of the failure of enzyme systems further along in the chain of reactions involving ammonia. An investigation of the mechanisms involved in the formation of urea, the Krebs-Henseleit sequence, in *S. mansoni*-infected mouse liver would probably be productive.

Additional evidence of an overall interference with liver function was seen in studies on the transaminase mechanism in liver homogenates (unpublished observations). In the alanine-to-glutamic acid system a decrease in activity of 30 per cent was found in nine cases. With corrections for the higher water content and the nonactive tissue in the infected liver, these results are still sufficiently significant to suggest an interference with many aspects of liver function.

Little can be said at this time about the factors leading to the death of the animal from schistosomiasis. A failure in ammonia metabolism would certainly contribute but much work needs to be done on other functions of the liver. If other liver activities are influenced in a manner similar to that suggested for amino nitrogen metabolism, a study of the various detoxication mechanisms in liver cells should give interesting results.

SUMMARY

Preliminary studies on the effects of *S. mansoni* infections in mice gave evidence of an increased liver size, an increased water content of the liver, a decreased oxidative deamination of amino acids, and a failure in ammonia metabolism. These results are discussed in relation to the structural changes in the liver that accompany the infection.

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MOLLUSCICIDING OPERATIONS IN AN ENDEMIC AREA OF SCHISTOSOMIASIS IN THE DOMINICAN REPUBLIC[1]

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In a study of the endemic area of schistosomiasis in the vicinity of Hato Mayor, Seibo Province, The Dominican Republic, Olivier, Vaughn and Hendricks (1952) found the snail host, *Australorbis glabratus*, only in two connected streams on the eastern margin of the town. The restricted distribution of the snail in these two streams suggested the possibility that transmission of schistosomiasis in the town could be controlled or even eradicated by treating the streams with a molluscicide. Accordingly, it was decided to treat the streams with sodium pentachlorophenate. Some of the results of this treatment are reported here.

Numerous chemicals have been tested for their molluscicidal activity both in the laboratory and in the field, and sodium pentachlorophenate is one of the more promising of the compounds tested. The chemical was field tested in Japan by Mc Mullen *et al.* (1948 and 1951), in Texas by Nolan and Berry (1949), and in Puerto Rico by Berry, Nolan, and Oliver-González (1950). Hunter *et al.* (1952) have reported actual control of the snail host of *Schistosoma japonicum* in Japan with this compound.

The two infected streams near Hato Mayor, the arroyos Paña Paña and Las Guamas, were described and mapped by Olivier *et al.* (1952). Both of the streams have a very small flow of water except during the rainy season. In the dry season the flow in the arroyo Paña Paña approximates 5 to 15 cubic feet per minute. Nevertheless, the volume of water in the stream at this season is large because of many shallow pools in the stream bed each containing from 200 to 10,000 cubic feet of water. The arroyo Las Guamas is much smaller than the Paña Paña. In

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the dry season this stream consists only of a series of small pools which may dry completely.

MATERIAL AND STREAM TREATMENT PROCEDURES

Sodium pentachlorophenate in one-ounce briquettes (Santobrite) was made available by the Monsanto Chemical Company through the Laboratory of Tropical Diseases, National Institutes of Health. Two lots were provided, one of which contained 79 per cent sodium pentachlorophenate and 11 per cent sodium salts of other chlorophenols while the other contained 75 per cent sodium pentachlorophenate and 13 per cent sodium salts of other chlorophenols. The remainder of the briquettes consisted of inactive ingredients. The chemical was used in the briquette form since it is safer and easier to handle in this form and therefore, more practical for large-scale field use.

Before the tests were made the streams were measured to determine the length and water volume of each. For later reference the pools and riffles were measured and numbered consecutively from the mouth upstream. The streams were considered as standing water for purposes of calculating the amount of chemical required since the stream flow was small in comparison with the volume of water.

Prior to the application of chemical, water samples were collected and tested by the method of Haskins (1951) for determining concentrations of chlorinated phenols. Following use of the chemical numerous water samples were taken from the treated area and tested by the method of Haskins. These samples were collected from a variety of locations including the margins of the pools and shallow and deep portions of the pools. Additional samples were taken from the outflows of pools below the treated area in order to follow the progress of the chemical downstream.

The snails were identified by Mr. R. Tucker Abbott of the U. S. National Museum. The fish were identified by Dr. L. P. Schultz and Dr. E. A. Lachner of the U. S. National Museum and Mr. Isaac Ginsburg of the U. S. Fish and Wildlife Service.

RESULTS

Preliminary test

Sodium pentachlorophenate was used in the arroyo Paña Paña in a series of tests during February and March, 1952. The first area to be treated was located below the areas where *Australorbis glabratus* had been found in significant numbers. In this test the objective was to determine in a preliminary way how the chemical should be applied and to acquire practice in the technic of testing water samples. The test area was 454 feet long and consisted of eight pools connected by short, rocky riffles (upper third of shaded portion of stream extending downward from Pool 39, Fig. 1). From the estimated volume of water in the test area it was calculated that 245 briquettes, if they dissolved completely and if the chemical were evenly distributed in the water, would produce a concentration of approximately 15 p.p.m. Each pool received the amount of chemical

required to treat it at the calculated concentration. Whole briquettes were distributed evenly on the bottom of four of the pools containing 1,400, 10,000, 1,300 and 600 cubic feet of water. Whole briquettes were distributed evenly on the bottom of the lower half of a fifth pool containing 2,000 cubic feet of water; the briquettes for the upper half of this pool were placed on the rocks in flowing water at the entrance to this pool. Dissolved chemical was sprayed on the surface

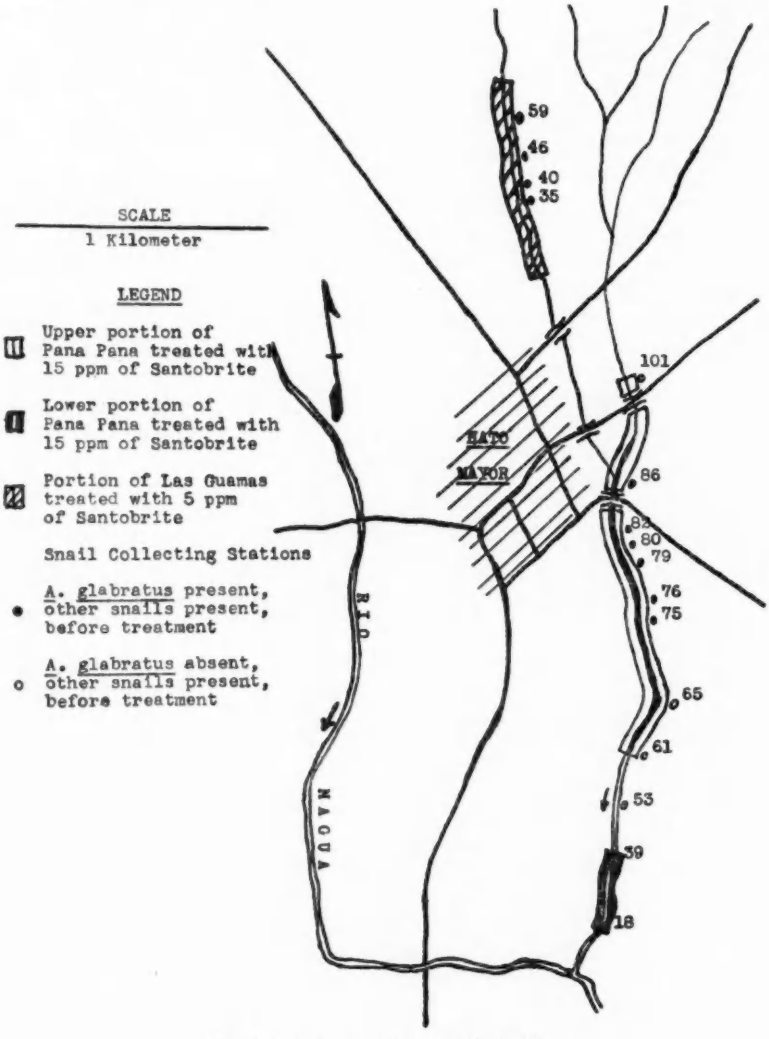

FIG. 1. Streams treated near Hato Mayor

of three of the pools containing 450, 30 and 300 cubic feet of water. Twenty-one water samples collected 2½ hours later contained from 2 to 10 p.p.m. of the chemical. In fifteen samples collected 18 hours after treatment, the concentrations ranged from 4 to 8 p.p.m.

Test I

For the initial test a major portion of the arroyo Paña Paña, including all of the stream known to be populated by *Australorbis glabratus* was treated. The test area was about 5,000 feet long and contained approximately 110,000 cubic feet of water, most of it in 43 pools in the stream bed (Pools 103–61, Fig. 1).

Prior to the treatment, ten stations along the course of the stream in and below the test area were selected for pretreatment snail counts (Fig. 1). One day before the treatment two experienced collectors searched for snails at each station for ten minutes and recorded the number and species of all snails collected (Table 1). The snails were then returned to the water where they were found. Following treatment these same collectors searched for snails in the same localities (Table 1).

All of the test area except one pool was treated by scattering briquettes of the chemical evenly in the stream bed. The briquettes sank to the bottom and there gradually dissolved. Sufficient chemical was used to provide a calculated 15 p.p.m. of dissolved molluscicide based on the volume of water and the assumption that all the chemical introduced into the stream would be dissolved and evenly distributed in the water. One pool (Pool 85), close to Hato Mayor, was heavily charged with garbage and other wastes and it was felt that there would be little chance that the chemical could become evenly distributed there if applied in the form of briquettes since diffusion would probably be very slow. Here dissolved chemical was sprinkled on the surface of the pool to produce a calculated concentration of 30 p.p.m. Six hours after introduction of the briquettes two men waded the length of the treated area to agitate the water and so speed the distribution of the chemical.

Sixty-eight water samples were collected and tested six hours after the treatment. Approximately the same number of samples for testing were also taken, usually from exactly the same places, one, two, three, four, six and eight days after the treatment. At six hours, in the pools treated with briquettes, the concentrations of the chemical varied widely, ranging from 2 to 18 p.p.m. In the pool treated with dissolved chemical the concentration in all parts was over 25 p.p.m. After one day samples from almost all pools treated with briquettes had from 2 to 10 p.p.m. of chemical but the pool treated with solution had 10 to 18 p.p.m.

The water from the heavily treated pool gradually passed downstream and one day after treatment concentrations of 20 to 25 p.p.m. were encountered in the four pools below the heavily treated pool (Pool 85). The next day the high concentrations (10 to 25 p.p.m.) were in the fourth to ninth pools (Pool 81–76) below the heavily treated pool, on the third day concentrations of 8 to 18 p.p.m. were concentrated in the sixth to fifteenth pools (Pools 79–70) below the heavily

TABLE 1

Living gastropods from snail collecting stations in the Arroyo Paña Paña and Arroyo Las Guamas before and after the application of sodium pentachlorophenate

A. Arroyo Paña Paña

POOL NUMBER	SNAILS COLLECTED BY TWO PERSONS DURING 10 MINUTE PERIOD				SNAILS COLLECTED BY TWO PERSONS DURING 15 MINUTE PERIOD					
	Before treatment		24 hours post treatment		3 weeks post treatment		5 months post treatment		6 months post treatment	
	*A.g.**	O.s.†	*A.g.*	O.s.	*A.g.*	O.s.	*A.g.*	O.s.	*A.g.*	O.s.
101	0	186	0	0	0	0	0	0	0	4
86	1	301	0	0	0	0	0	3	0	16
82	28	141	0	0	0	0	0	0	0	1
80	32	139	0	0	0	0	0	0	0	0
79	52	328	0	0	0	0	0	15	0	1
76	20	426	0	0	0	0	0	2	0	1
75	3	426	0	0	0	0	0	1	0	1
65	0	172	0	0	0	0	0	13	0	7
61	0	146	0	0	0	0	0	0	0	3
53‡	0	105	0	100	0	0	0	45	0	0

B. Arroyo Las Guamas

POOL NUMBER	COLLECTION PERIOD IN MINUTES USED BY ONE PERSON		SNAILS COLLECTED BEFORE TREATMENT		SNAILS COLLECTED 24 HOURS POST TREATMENT		SNAILS COLLECTED 1 WEEK POST TREATMENT	
	Before treatment	After treatment	*A.g.*	O.s.	*A.g.*	O.s.	*A.g.*	O.s.
59	10	15	0	27	0	0	0	0
46	10	15	19	3	0	0	0	2
40	10	15	16	7	0	0	0	0
35	5	10	40	0	0	0	0	2

* *Australorbis glabratus.*

† Other species (*Physa cubensis*, *Tropicorbis riisei*) (and *Drepanotrema anatinum* in 5 and 6 months post treatment collections).

‡ About 1,000 feet below the treated area.

treated pool. Thus much of the treated area was eventually subjected to relatively high concentrations of the chemical during at least a part of the week following treatment. However, the seven pools in the lowest part of the treated area never had concentrations over 7 p.p.m. Water samples taken downstream from the treated area (below Pool 61) over the eight day period indicated that the chemical moved slowly downstream (Table 2) but the concentration of the chemical in the untreated area never exceeded 4 p.p.m.

The efficacy of the chemical in killing the snails in the stream was judged by the results of searches for snails after treatment. One day after treatment no living snail was found at any of the nine collecting stations within the treated area. All ten stations were checked again three weeks, five months and six months after treatment. Results appear in Table 1.

Observations were made on snails living in Pools 60–40 to determine the effects

TABLE 2

Downstream flow of sodium pentachlorophenate in Arroyo Paña Paña from Pool 60 to Pool 40

POOL NUMBER	LENGTH IN FT.	VOLUME CU. FT.	PARTS PER MILLION OF SODIUM PENTACHLOROPHENATE IN POST TREATMENT WATER SAMPLES COLLECTED AT THE FOLLOWING INTERVALS:					
			1st Day	2nd Day	3rd Day	4th Day	6th Day	8th Day
60	105	1,470	3	3	4	4	3	3
59	177	3,842	—	2	2	4	3	−2*
58	67	538	—	2	2	3	3	−1
57	31	581						
56	230	4,140						
55	105	5,250	0	−1	−2	3	3	−2
54	290	10,030	0	−1	−1	−2	3	—
53	310	7,480	—	—	−1	−1	2	−1
52	53	222						
51	40	2,100	0	—	−1	−1	2	−1
50	98	1,634	—	—	−1	−1	−2	−1
49	43	153	0	—	0	T	−2	−1
48	100	2,000						
47	79	474						
46	50	675						
45	50	675						
44	60	90	—	—	—	T	−2	−1
43	47	1,974						
42	147	3,212	—	—	—	0	−1	−1
41	138	624						
40	88	1,816	—	—	—	—	−1	−1
Totals.....	2,308	48,980						

—No reading made.

* Bar preceding number indicates less than number but greater than next lower whole number.

T—Trace.

of the chemical as it moved downstream from the treated area. Two days after treatment, living snails were found in Pools 60 and 54 but both living and newly dead snails were found in Pool 54. On the third day, one living snail was found in Pool 60 but all were dead in Pools 54 and 53. All were alive in Pool 50. On the fourth day, two living snails were seen in Pool 60, all were dead in 54 and 53, many were dead in 50 and all were alive in 49 and 45. Six days after treatment, all snails were dead in Pools 60, 51, 49 and 45. A few were alive in 50 and all were alive in 41 and 40. After seven days, all snails were dead as far downstream as Pool 40 where both living and dead snails (*Physa cubensis* and *Tropicorbis riisei*) were found. On the eighth day, almost all the snails (*Physa cubensis* and *Tropicorbis riisei*) in Pool 40 were dead. Table 2 shows the concentrations of the chemical in the pools when these observations were made.

Test II

In Test I, except for the pool treated with solution of the chemical, the actual concentrations of the chemical in the water were smaller than predicted on the

basis of the volume of water and amount of chemical used. One possible reason for this is that the chemical may have been lost in the thin layer of mud on the bottom of the pools where the briquettes lay as they dissolved.

In the second test, in an effort to find a way to use the chemical more efficiently, almost all the briquettes were placed on the rocks in the flowing water between pools. Here the briquettes could dissolve speedily and the solution could pass rapidly into the pool and be dispersed. Moreover, with this method the chemical could be applied faster and more easily because the stream bed had to be entered only at the ends of the pools and the briquettes could be poured into the riffles whereas with the other method they had to be distributed evenly in the stream bed.

The number of briquettes needed for each pool or series of pools was calculated in advance, placed in a numbered bag and carried to the stream on the day of treatment. The portion of the stream treated was 1,500 feet long and contained about 40,500 cubic feet of water in 21 pools (Pools 39–18, Fig. 1). This part of the stream was below the area treated in Test I and was treated two weeks after Test I was begun. Tests of the water prior to this treatment showed that there was a slight residual of the chemical in the water since trace quantities were present in the water samples. Sufficient chemical was placed in the stream so that if it all dissolved and were evenly distributed in the water the concentration would be 15 p.p.m. Two of the pools were so large that it was thought that chemical placed only in the entrance of the pool might not be distributed evenly to all parts of the pools. Therefore, half of the required amount was suspended in the middle of each pool from a tripod. Since this part of the stream held no significant snail population, no study of the molluscicidal activity of the chemical could be made.

Immediately after the chemical was introduced it was seen to dissolve rapidly. The briquettes placed in the riffles between pools dissolved within two hours and those hung in the middle of the pools were almost all dissolved in six hours. From Pools 64 to 75 water samples were taken in and below the treated area six hours after introduction of the chemical and additional samples were taken, usually in exactly the same places, one, two, three, four and six days after treatment.

At six hours the concentrations of the chemical in the treated portion of the stream ranged from 3 to 30 p.p.m. and averaged 15 p.p.m. After one day, with the exception of the samples from the upper two pools which had, of course, received much untreated water from above, the range was from 6 to 25 p.p.m. and the average was 12 p.p.m. After two days, the range was 3 to 18 p.p.m. and the average was 9 p.p.m. One day later, the range was 3 to 18 p.p.m. and the average was 8 p.p.m. Before the samples were taken on the fourth day, heavy rain intervened and diluted the water. Only trace quantities of chemical were found in the treated area thereafter.

Table 3 shows the concentrations of the chemical used in this test as it passed downstream from the treated area. Over a period of six days the chemical passed downstream about 1,000 feet through about 20,000 cubic feet of water. All the pools in this area had concentrations of 4 p.p.m. or more of chemical at some time during the six days.

TABLE 3

Downstream flow of sodium pentachlorophenate in Arroyo Paña Paña from Pool 17 to Pool 1

POOL NUMBER	LENGTH IN FT.	VOLUME CU. FT.	PARTS PER MILLION OF SODIUM PENTACHLOROPHENATE IN POST TREATMENT WATER SAMPLES COLLECTED AT THE FOLLOWING INTERVALS:				
			1st Day	2nd Day	3rd Day	4th Day	6th Day
17	80	160	10	18	20	2	T
16	30	810	7	10	10	2	—
15	20	300					
14	20	300					
13	50	675	7	12	12	3	−2*
12	72	317					
11	30	300					
10	50	403	—	10	12	5	−2
9	103	5,243	—	7	8	5	2
8	213	4,345					
7	42	168	—	−1	6	8	−2
6	32	256					
5	24	48					
4	136	2,720	—	T	3	6	−2
3	38	998					
2	30	150	—	0	T	8	3
1	90	2,520	—	0	T	10	4
Totals.....	1,060	19,713					

—No reading made.

* Bar preceding number indicates less than number but greater than next lower whole number.

T—Trace.

Test III

When the arroyo Paña Paña was treated, the arroyo Las Guamas was almost completely dry. In August, 1952, however, the latter stream bed approximately 3,000 feet long contained water in a series of 70 standing pools containing approximately 9,000 cubic feet of water with no appreciable flow between the pools (Fig. 1). However, the total water volume was subject to marked fluctuations due to daily rainfall. These pools were numbered upstream from the upper end of the concrete drain which carries the water of this stream into the arroyo Paña Paña.

On the day before treatment, four stations were selected in the stream for pretreatment snail counts. An experienced collector searched for snails at each station for ten minutes except at Pool 35 where a five minute period was used to record the number and species of all snails collected (Table 1). The snails were immediately returned to the pool from which they had been taken. These same stations were searched for snails by the same collector (Table 1) one day and also one week after treatment.

In the absence of flowing water, these pools were measured and then treated with chemical in solution in amounts calculated to produce 5 p.p.m. of dissolved chemical (Fig. 1). The solution was sprinkled on the surface of the pools and after

the entire stream had been treated one man waded the length of the treated area to stir the water and speed the distribution of the chemical. In contrast to the arroyo Paña Paña the stream bed of the arroyo Las Guamas was practically all mud bottom and the mud was three to six inches deep. The wading of the stream after treatment made the water very turbid and this turbidity persisted for at least two days after treatment in part of the stream.

Thirty water samples were collected and tested one, two, three and four days after treatment. Of the water samples collected the day after treatment, two gave readings of 2 p.p.m. and two gave trace readings while all others were negative. On the next day, six water samples tested indicated traces of chemical and three indicated 3 p.p.m. All other samples were negative. On the third day five test samples indicated 3 p.p.m. and six samples gave trace readings for the chemical, indicating the presence of the chemical from Pool 9 upstream to Pool 64. Four days after treatment four scattered water samples of the thirty collected gave trace readings of the chemical while all others were negative.

One day after treatment no living snail was found at any of the collecting stations in this stream. One week later no *Australorbis glabratus* were found but a few *Physa cubensis* were present (Table 1).

Notes on other aquatic life

The best evidence concerning the effect of the chemical on other aquatic life in the streams came from Test I. Apparently all the fish (*Gobiomorus dormitor*, *Awaous taiasica*, and *Agnostomus monticola*) in the treated pools were killed very quickly. In the portion of the stream below the treated area dead fish were found in all pools where the chemical concentration reached 1 p.p.m. and there was evidence that they may have been killed by even lower concentrations. In one pool when no more than trace amounts of chemical were detected in test water samples there were many dead fish in the pool. Leeches and shrimps were also dead yet snails and insect larvae were alive. Two days later, about 2 p.p.m. of chemical were present in test water samples from this pool and at this time all the snails and many of the insect larvae were dead.

DISCUSSION

Sodium pentachlorophenate drastically reduced the snail population of the two streams near Hato Mayor. No living snails were found in the treated areas one day after treatment and in the portion of the stream where *Australorbis glabratus* had been very plentiful (Test I) no snail of this species was found six months after the single application of the chemical. In a large part of the latter area the concentration of the chemical reached a level of over 10 p.p.m. and was as high as 25 p.p.m. in some places. Thus, many of the heavily infested parts of the stream were treated with fairly high concentrations. However, it was also shown in Test I that the chemical could kill snails in low concentration since snails in pools below the treated area were killed even though the concentration of the chemical did not exceed 2 p.p.m. Moreover, in the arroyo Las Guamas no living *Australorbis glabratus* were found up to one week after treatment even though the detectable quantity of the chemical after treatment was very low.

These apparently successful tests are not to be interpreted as indicating that the vectors of schistosomiasis were eradicated from the streams in question. Some snails probably were not reached by the chemical and may repopulate the streams. The gastropod fauna present in the five and six-month post-treatment collections (Table 1) were primarily all small planorbid snails representing species also present in the portion of the stream above the treated area. This apparent repopulation of the treated portion of the stream may be due to an infiltration by these snails into the treated portion of the stream from above or to only partial eradication of these species by the single application of sodium pentachlorophenate. Nevertheless, transmission of schistosomiasis at Hato Mayor was probably interrupted for a considerable time.

In the arroyo Paña Paña, which has a small flow and a large volume of water, the chemical persisted for at least eight days at relatively high levels indicating that it was not readily neutralized or dissipated into the stream bed. One consequence of the persistence of the chemical was that significant quantities passed downstream and affected the snail population there. In two of the tests in the arroyo Paña Paña the chemical reached a downstream concentration of 2 p.p.m. or more for distances equal in length to 46 and 70 per cent of the original areas treated. Effective downstream penetration of sodium pentachlorophenate can be used to advantage in planning for its use in flowing water. Once the effective downstream penetration of the chemical is known for a given stream the chemical need be applied only at intervals along the stream with resultant saving of time and labor.

Under the conditions of the tests just described the method of placing the chemical in the rapidly flowing water between pools of the arroyo Paña Paña was preferable to the other two methods used. The chemical was distributed easily and rapidly without the use of special equipment, yet, on the whole, the concentrations of chemical obtained were very good. Distribution of the briquettes in the bottom of the pools was more laborious and produced lower concentrations. Application of the chemical in solution was efficient but laborious and slow.

Treatment of the arroyo Las Guamas with the chemical in solution suggested that some modification of this method would be required in subsequent treatment of streams which have a mud bottom. Wading of such streams following application of chemical should be omitted to prevent the increased turbidity which may have reduced the concentration of sodium pentachlorophenate. It should be noted in this connection that Dobrovolny and Haskins (1953) showed experimentally that mud reduced the concentration of the salts of pentachlorophenol in solution. The absence of *Australorbis glabratus* one week after treatment indicates that molluscicidal action had occurred even though the detectable sodium pentachlorophenate was in low concentration.

Although introduction of the chemical only into the rapidly flowing portions of the arroyo Paña Paña was efficient and relatively easy, the resulting concentrations of the chemical in the water samples varied considerably. This inequality of distribution of the chemical is to be expected and sufficient amounts should be used to provide at least a minimum effective concentration in all parts of the stream. What this effective minimum concentration is under field conditions

remains to be determined and it may differ somewhat from stream to stream, but in any event it will be dependent upon the length of time that the concentration is maintained. Thus, if the chemical is present at a given location in a stream for only a short time a high concentration will be necessary but if the chemical persists for a longer period a relatively lower concentration might be equally effective.

SUMMARY

Destruction of the intermediate host of *Schistosoma mansoni*, *Australorbis glabratus*, in the endemic area at Hato Mayor in the Dominican Republic was accomplished by using sodium pentachlorophenate (Santobrite) in briquette form. A single application of sodium pentachlorophenate at an estimated rate of 15 p.p.m. eradicated *Australorbis glabratus* from the arroyo Paña Paña, a flowing stream, for a period of six months. A single application of the chemical at an estimated rate of 5 p.p.m. destroyed *Australorbis glabratus* in the arroyo Las Guamas, a series of connected pools with negligible flow, as evidenced by examination of the stream one week after treatment. Several methods of applying sodium pentachlorophenate, using the briquette form, were used and evaluated by colorimetric tests of water samples. Higher concentrations of sodium pentachlorophenate were required to destroy invertebrates in the arroyo Paña Paña than were required to destroy fish.

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MORPHOLOGIC VARIATIONS OF LARVAE OF THE *SCUTELLARIS* GROUP OF *AEDES* (DIPTERA, CULICIDAE) IN POLYNESIA

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The *scutellaris* group of *Aedes* (Stegomyia), which ranges from the eastern part of the Australasian Region to the eastern part of the Oriental Region, includes species which have been incriminated as important vectors of human filariasis and dengue. This complex now contains 17 species, all of which are similar morphologically. The various species are differentiated primarily by the structure of the male terminalia, although in certain species the coloration characters of the adults are of use.

Larvae of only one species, *Aedes horrescens* Edwards, have been considered as disinctive (Edwards, 1935). This species was originally distinguished from other members of the *scutellaris* group by the prominent stellate setae of the larvae, which made them appear hairy (hence the name *horrescens*). These hairy larvae have been found primarily in tree holes (Paine, 1943; Lever, 1944 and 1945) in contrast to most species of the *scutellaris* group which utilize a wide variety of small containers as breeding sites.

Since the work of Bahr (1912), members of the *scutellaris* complex have been recognized as important vectors of nonperiodic filariasis in Polynesia. At the present time, four species of this group are known to occur in endemic areas of nonperiodic *Wuchereria bancrofti*.

Aedes polynesiensis Marks is a widespread species in Polynesia and a proven vector of *W. bancrofti*.

Aedes tongae Edwards is a suspected but unproven vector of *W. bancrofti*. It is the only species of the *scutellaris* group known to occur in the Tonga Islands (an endemic area of *W. bancrofti*).

Aedes horrescens Edwards is reported to be an unsuitable host for *W. bancrofti* (Manson-Bahr and Muggleton, 1952). It is known only from the Fiji Islands.

Aedes pseudoscutellaris Theobald is also known only from the Fiji Islands. The

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ability of this mosquito to serve as a host of *W. bancrofti* is unknown since *A. polynesiensis*, which also occurs in Fiji, has only recently been recognized as a distinct species (Marks, 1951), and hence it is not known with which species of the *scutellaris* group previous workers in Fiji had dealt. *A. polynesiensis* is known to be a vector of *W. bancrofti* because it is the only species recognized from the Samoa Islands where it has been incriminated, under various synonyms, by several epidemiologic investigations (see Byrd *et al.*, 1945).

Early in the course of studies on filariasis in the Society Islands, the senior author encountered two types of larvae of the *scutellaris* group, a common form conforming to the description of *A. polynesiensis*, and a less common hairy variety, which was found primarily in tree holes, conforming in most respects to the description of *A. horrescens*. Meanwhile, Lt. Leo A. Jachowski, U. S. N., during the course of his studies on filariasis, also encountered hairy larvae of the *scutellaris* group on several occasions in the Samoa Islands (1951).

FIELD OBSERVATIONS IN THE SOCIETY ISLANDS

As a part of the assessment of the importance of imagoes associated with the hairy type of larvae in the transmission of *W. bancrofti* in the Society Islands, an attempt was made to establish a laboratory colony of these mosquitoes in order to facilitate infection experiments. Approximately 165 fourth instar larvae of the hairy type were collected and examined individually to be certain that all were typical. Adult females which developed from these larvae were allowed to feed on an individual having microfilariae of *W. bancrofti* in his peripheral blood and were then given the opportunity to lay eggs. After these eggs had hatched, the resulting larvae were reared on a diet of powdered bread crumbs. When these larvae had developed to the fourth instar they were examined and, surprisingly, they resembled not the hairy larvae of the preceding generation, but rather, the non-hairy larvae of *A. polynesiensis*.

The development of *W. bancrofti* in those mosquitoes which had fed on the infected donor was similar both qualitatively and quantitatively to that which occurred in mosquitoes reared from non-hairy larvae (Rosen, 1951).

It was also observed that when young hairy larvae (late second or early third instar) were removed from their natural habitat and reared in the laboratory on powdered bread crumbs, they became relatively less hairy by the time they attained the fourth instar.

Further field observations revealed that some tree holes contained larvae intermediate between the hairy and the non-hairy types. Moreover, a single tree hole sometimes contained a range of larvae from typical hairy to typical non-hairy types. Furthermore, a tree hole containing only hairy larvae, might, a few weeks later, contain only non-hairy larvae. In general, it seemed as if hairy larvae were found most frequently in tree holes which contained a large amount of debris. Occasionally, hairy larvae were found in other containers, such as rock holes, in which the larval environment seemed similar to that in tree holes.

The preceding observations suggested that the hairiness of certain larvae of the *scutellaris* group in the Society Islands was the result of a peculiar larval

environment occurring most frequently in tree holes. This possibility was further explored by the following experiment. Water and debris were collected from a tree hole which harbored numerous hairy larvae in all stages of development. All mosquito larvae were removed and the remaining contents of the tree hole were placed in three enamel pans. Both debris and water from the tree hole were placed in each of two pans, and only water (which had been filtered through ordinary filter paper) was placed in the third. Tap water and brewer's yeast were placed in a fourth pan. About 50 mature eggs which had been laid by adults reared from non-hairy larvae were placed in each of the pans except one of the two containing both debris and water from the tree hole. The pan in which no eggs were placed was used as a control to be certain that no unhatched eggs, which might have been laid in the tree hole in nature, remained in the debris. All pans were placed in a bobbinet cage to prevent adult mosquitoes from laying eggs in them.

Almost all eggs placed in the three pans hatched. However, the larvae in the two pans containing tree hole contents grew slowly, as compared with those in the tap water and yeast, and eventually many of them died. This seemed to be due to a lack of larval food. On the fourth day after hatching, larvae in the pan with both debris and water from the tree hole were definitely identifiable as of the hairy type. Daily examination of larvae in all three pans was continued until the ninth day after hatching. At no time were larvae of the hairy type found either in the pan with tap water and yeast or in the pan with filtered tree hole water. No larvae were found in the control pan with both debris and water from the tree hole. After nine days, about 50 eggs from the same lot as those referred to above were placed in this control pan along with a small amount of brewer's yeast. The eggs hatched and the larvae grew rapidly but no indication of hairiness could be found.

MORPHOLOGIC CHARACTERISTICS OF LARVAE AND ASSOCIATED ADULTS

Morphologic study of larvae of the *scutellaris* group was continued at the Johns Hopkins University, School of Hygiene and Public Health. The material examined included series of hairy and non-hairy larvae and associated adults from the Society Islands; several series of hairy and non-hairy larvae and associated adults from the Samoa Islands; several series of hairy and non-hairy larvae from the Fiji Islands (one series of hairy larvae was associated with adults); a single series of larvae and associated adults from the Tonga Islands; larvae and associated adults from the laboratory colony of *A. pseudoscutellaris* maintained at the London School of Tropical Medicine and Hygiene (see Marks, 1951); and a male and several larvae of the series of *A. horrescens* from which the type material of this species had been chosen.

It was found that the male terminalia of adults associated with both the hairy and the non-hairy types of larvae from both the Society Islands and the Samoa Islands were identical and that they conformed to the published descriptions and illustrations of *A. polynesiensis* (Farner and Bohart, 1945). Twelve collections containing 75 larvae, mostly of the hairy variety, were examined from the Society Islands. There were 12 hairy and 3 non-hairy larval skins which were

individually associated with *A. polynesiensis* males and 4 *A. polynesiensis* males which had been bred out from hairy larvae collected with other hairy larvae which were preserved. Six collections containing 74 larvae, mostly of the hairy variety, were examined from the Samoa Islands. There were 16 non-hairy, one hairy, and one intermediate type larval skins which were individually associated with *A. polynesiensis* males. In addition, there were mass associations of 62 *A. polynesiensis* males with non-hairy larvae and 9 males of this species with hairy larvae.

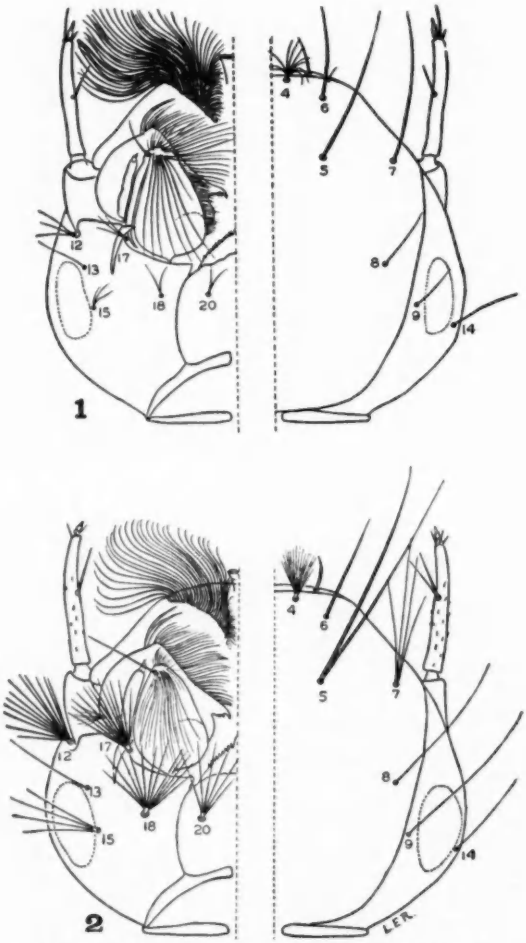

FIG. 1. *Aedes polynesiensis*, head of non-hairy larva
FIG. 2. *Aedes polynesiensis*, head of hairy larva

The male terminalia and scutal markings of 6 adults (3 males and 3 females) associated with a series of 9 hairy larvae from the Fiji Islands were as described for *A. pseudoscutellaris* (Marks, 1951). Unfortunately, the adults were not individually associated with larval skins; however, they were bred out from hairy larvae taken from the same tree hole at the same time as the 9 larvae which were preserved. The identification of *A. pseudoscutellaris* was based on the presence of a line of pale scales on the anterolateral margins of the scutum and on the presence of a row of specialized setae on the basal lobe of the male terminalia (Fig. 10).

Another series of hairy larvae (11 specimens) from the Fiji Islands was also tentatively identified as *A. pseudoscutellaris* on the basis of the ratio between the length of the lower and the upper pairs of anal papillae (Marks, 1951). This ratio is higher (i.e. closer to one) in *A. pseudoscutellaris* than in *A. polynesiensis*,

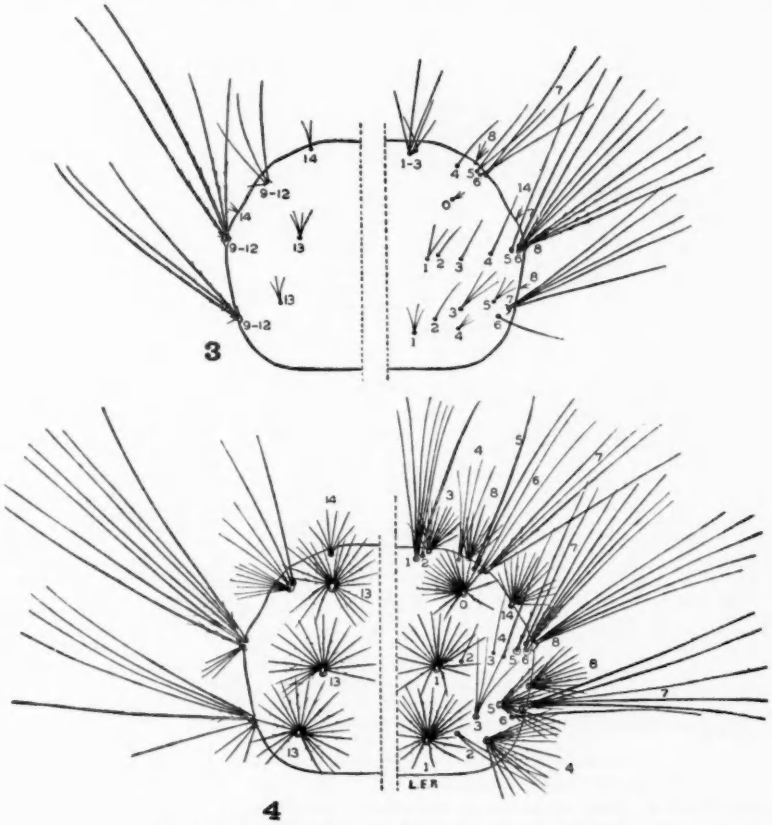

FIG. 3. *Aedes polynesiensis*, thorax of non-hairy larva
FIG. 4. *Aedes polynesiensis*, thorax of hairy larva

and is also higher than that described for the larvae of *A. horrescens* (Edwards, 1935). Larvae from the colony of *A. pseudoscutellaris* from the London School of Hygiene and Tropical Medicine (10 specimens were studied in detail) were of the non-hairy variety, as was another series of larvae from the Fiji Islands (14 specimens) tentatively identified as *A. pseudoscutellaris* on the basis of the anal papillae.

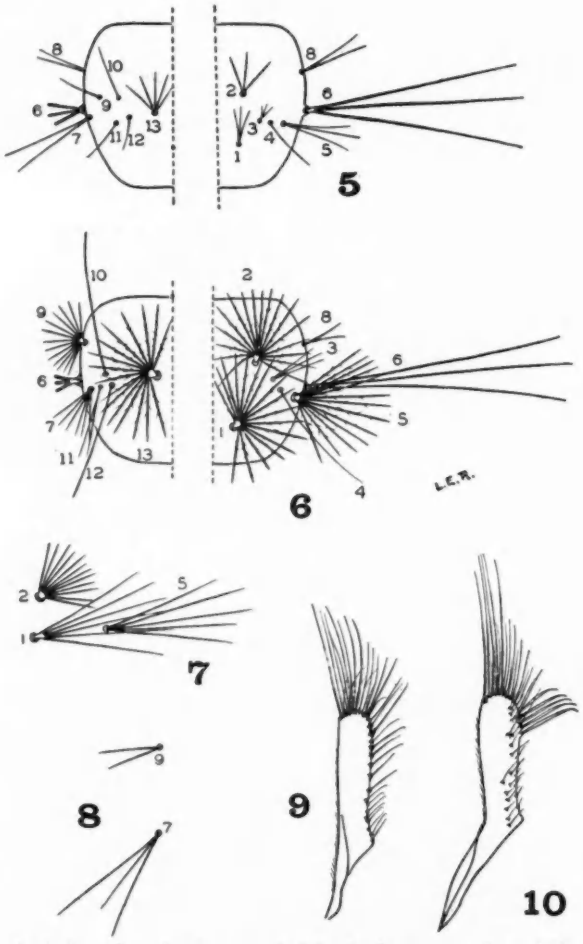

FIG. 5. *Aedes polynesiensis*, second abdominal segment of non-hairy larva
FIG. 6. *Aedes polynesiensis*, second abdominal segment of hairy larva
FIGS. 7 AND 8. *Aedes polynesiensis*, variations in certain setae of the second abdominal segment of hairy larvae.
FIG. 9. *Aedes polynesiensis*, basal lobe (lateral view) of male terminalia
FIG. 10. *Aedes pseudoscutellaris*, basal lobe (lateral view) of male terminalia

The single series of larvae (21 specimens) from the Tonga Islands was non-hairy and the male terminalia of the associated adults were as described and illustrated for *A. tongae* (Farner and Bohart, 1945).

Eight larvae and one male from the type locality of *A. horrescens* (Taveuni, Fiji Islands) were obtained through the British Museum. These specimens had been collected in 1933 and 1934 by R. W. Paine, and according to Mattingly (1953) the 1934 collection is the one from which the type material was bred and is also the source of the single male which we have examined.

The larvae were indistinguishable from hairy larvae of *A. polynesiensis* (they were distinguishable from *A. pseudoscutellaris* on the basis of the anal papillae

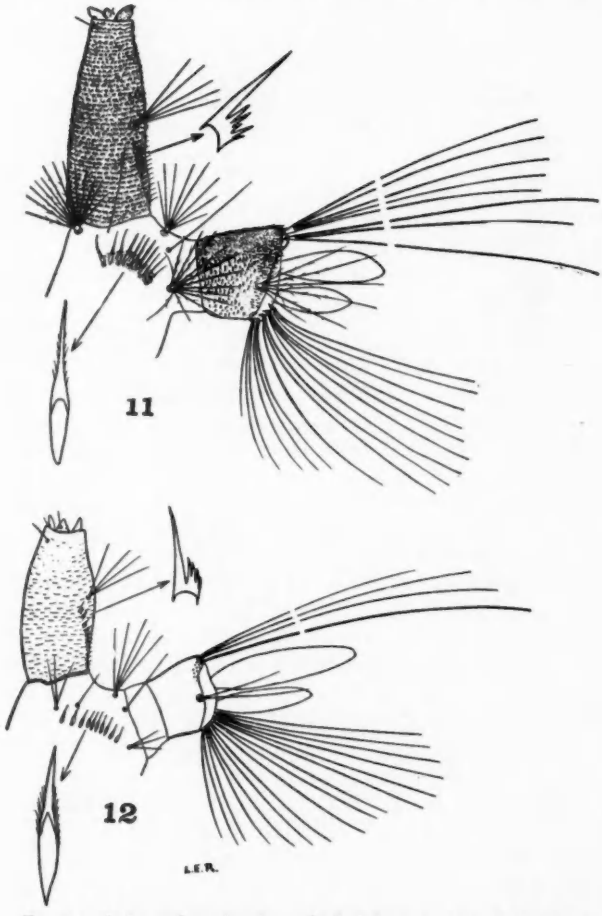

FIG. 11. ***Aedes polynesiensis*, end of abdomen of non-hairy larva**
FIG. 12. *Aedes polynesiensis*, end of abdomen of hairy larva

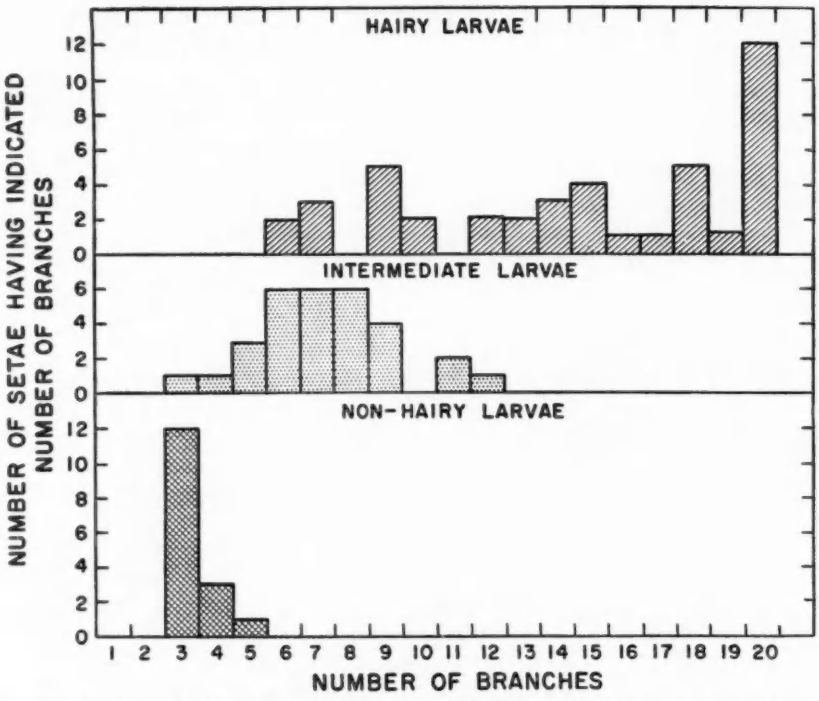
HAIRY LARVAE
INTERMEDIATE LARVAE
NON-HAIRY LARVAE
NUMBER OF SETAE HAVING INDICATED NUMBER OF BRANCHES
NUMBER OF BRANCHES
0 2 4 6 8 10 12
0 2 4 6
0 2 4 6 8 10 12
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20

FIG. 13. Frequency distribution of the number of branches of abdominal seta 2 of three collections of fourth instar larvae of *Aedes polynesiensis*.

as mentioned above). The terminalia of the single male were distinctly different from those of the other Polynesian species of the *scutellaris* group and were as illustrated for *A. horrescens* by Stone and Farner (1945).

The differences between the extreme hairy and non-hairy larvae of *A. polynesiensis* are illustrated in Figures 1–8, 11, and 12. Table 1 indicates quantitatively the wide range of variation which was observed in the branching of certain selected setae of the larvae of *A. polynesiensis* and *A. pseudoscutellaris*. Each of the series of larvae described in Table 1 represents a single larval collection from a single breeding site. In making these collections, no attempt was made to obtain a random sample of all larvae present; rather, in the case of hairy larvae, the hairiest specimens were usually selected. Figure 13 presents data in greater detail for a single seta. As shown in Figures 1–8, 11, and 12, the differences between larvae of the same species was by no means limited to the particular setae chosen for illustration in Table 1 and Figure 13. In general, setae of the hairy larvae were thicker, longer, and had more branches than did the corresponding setae in the non-hairy larvae, although some setae varied more than others. In addition, other parts of the integument of the hairy larvae, such as the siphon and anal saddle, were

TABLE 1

The variation in the number of branches of certain setae of the fourth instar larvae of A. polynesiensis *and* A. pseudoscutellaris

SPECIES	LOCALITY	MESOTHORACIC—1			ABDOMINAL*—2			LATERAL HAIR OF ANAL SADDLE		
		M.N.B.	R.N.B.	N.S.E.	M.N.B.	R.N.B.	N.S.E.	M.N.B.	R.N.B.	N.S.E.
A. polynesiensis	Tahiti†	3.0	2–4	16	3.3	3–5	16	2.1	2–3	16
	Samoa	3.2	2–4	17	3.3	3–4	12	2.0	2	1
	Samoa	3.2	2–5	17	2.9	2–4	18	3.0	3	3
	Tahiti	3.2	2–5	15	4.5	3–7	14	2.8	2–4	15
	Samoa	3.3	2–6	17	4.9	2–7	20	3.2	2–5	15
	Tahiti	3.0	2–4	7	3.7	3–5	6	3.0	2–4	7
	Tahiti	3.6	2–4	12	4.0	3–6	9	3.1	2–5	9
	Tahiti	6.7	3–9	7	5.4	4–7	8	3.8	3–4	4
	Tahiti	6.2	4–7	11	11.3	8–16	14	4.4	3–7	14
	Tahiti	5.2	3–9	29	7.3	3–12	30	3.4	2–5	29
	Tahiti	4.9	3–9	10	8.0	5–11	11	3.2	2–5	12
	Tahiti	7.9	4–15	8	8.4	4–15	11	3.9	3–6	11
	Samoa	7.1	2–12	10	11.7	2–20	13	3.0	2–4	10
	Samoa	10.9	3–25±	42	15.8	6–25±	43	4.6	2–9	42
	Samoa	19.5	4–25±	25	20.9	6–25±	24	6.4	3–12	27
A. pseudoscutellaris	Fiji	2.9	2–5	20	2.7	2–5	20	2.2	2–3	19
	Fiji	3.2	2–5	20	2.7	2–5	27	2.3	2–3	13
	Fiji	5.1	3–6	16	9.1	6–15	20	4.2	3–6	21
	Fiji	6.7	3–9	11	9.2	6–13	15	4.9	4–8	17

M.N.B. Mean number of branches.
R.N.B. Range number of branches.
N.S.E. Number of setae examined.
* Second abdominal segment.
† Society Islands.

also more heavily pigmented than were corresponding parts of the non-hairy larvae.

CONCLUSIONS

At least two species of the *scutellaris* group, *A. polynesiensis* and *A. pseudoscutellaris*, other than *A. horrescens*, can have hairy larvae under certain environmental conditions. *A. horrescens* remains as a distinct species, not because of the hairiness of the larvae by which it was detected and for which it was named, but rather because of the characteristics of the male terminalia.

Although the environmental factor responsible for the hairiness of larvae of *A. polynesiensis* was not elucidated, in the Society Islands it apparently occurs most commonly in tree holes, though not in all tree holes, or a majority of tree holes, or even in the same tree hole at all times. In the Samoa Islands, Jachowski (1951) encountered hairy larvae in various types of artificial containers; all of these, however, contained a considerable amount of debris. As demonstrated in

the experiments cited above, the factor seems to be associated with the debris in the breeding site but evidently is not solely the result of the physical presence of this debris.

Since Manson-Bahr and Muggleton (1952), in reporting that *A. horrescens* was an unsuitable host for *W. bancrofti*, based their identification of the mosquitoes on the hairiness of the larvae, and since it has now been shown that the other two species of the *scutellaris* group which are known to occur in the Fiji Islands can also have hairy larvae, it is not clear with which species they dealt.

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URBAN FLY DISPERSION STUDIES WITH SPECIAL REFERENCE TO MOVEMENT PATTERN OF *MUSCA DOMESTICA*

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During recent years, the dispersal habits of flies have been the subject of study by a number of workers (Lindquist *et al.*, 1951; Yates *et al.*, 1952; Schoof *et al.*, 1952; Schoof and Mail, 1953; and Quarterman, *et al.*, unpubl.). These investigations established that the major portion of house fly dispersion in a community falls within one mile of the release point although movement can and does occur to distances of 2 to 7 miles. However, the distance that flies migrate is only one measure of their possible significance in disease transmission or in creating control problems some distance from their point of origin. A second, and perhaps more important, criterion is the manner in which the flies accomplish their movement to these distant sites. Does the fly arrive at an ultimate destination merely as a result of haphazard wandering or is its course of dispersion essentially a straight-line movement? This paper describes an attempt to gain an insight into this aspect of fly migration.

METHODS

The flies utilized in this test were collected by means of traps at several sites of copious fly production in the vicinity of Phoenix, Arizona. All specimens were transported to the field station where tagging of the flies with P-32 was accomplished by feeding them a radioactive milk solution. The latter consisted of 1 millicurie of P-32 (phosphoric acid) per liter of milk solution (milk, honey and water). The feeding period extended for 24 hours, at the end of which sample checks indicated that more than 95 per cent of the flies were radioactive. *Musca domestica* yielded counts of more than 3,000 per minute, and the readings for blow flies ranged as high as 5,000 per minute. At the end of the feeding period, the approximately 171,000 tagged specimens were transferred to the liberation site A (Fig. 1) and released at dusk on October 30, 1952.

For a two-day period following the liberation of the tagged specimens at site A, 15 fly traps were operated at each of 3 stations located 0.5 mile from the release site (Figure 1, X, Y, Z). At each station, the traps were distributed over an area of 2 to 5 blocks. Flies captured at station X were dusted with a violet dye[1] and then released; the same operation was conducted at stations Y and Z except that green[2] and red dyes[2] were employed. During the two-day period, several individual lots of specimens received the dye treatments.

To recapture the dyed, radioactive flies, 70 traps baited with chicken entrails were dispersed within a one-mile arc centered on release point A (Figure 1). The

[1] Calcogas Violet Special—American Cyanamid Co.

[2] Calcogas Green 0-9660 Special and Calcogas Oil Red N-1700—Pylam Products Co., Inc.

RECOVERY OF RADIOACTIVE *Musca domestica* AND *Phaenicia spp.* LIBERATED AT PRIMARY RELEASE SITE "A"

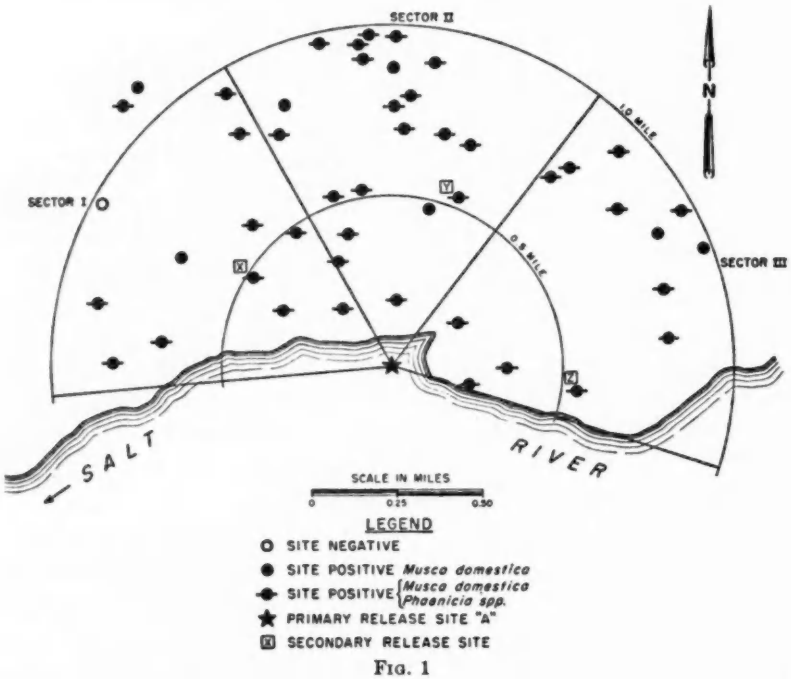

FIG. 1

location of the individual trap was based primarily upon the suitability of the site as an attractive point for house flies. In some instances, it was necessary to cluster 2 to 4 traps within a confined area to insure adequate recovery of specimens. Arrangement of collection sites was designed to afford adequate coverage of the areas encircling each of the secondary release points. Because the number of dyed, radioactive specimens available in the area was considered to be of a minimum quantity, the number of traps within the area was increased to three times that employed in earlier studies. Collection of flies was made 2, 4, 6, and 9 days after the last date on which dusting of specimens had occurred.

The test area encompassed an urbanized substandard residential zone south of Phoenix, Arizona. This section was selected chiefly because it offered a relatively homogeneous extent of sites highly attractive to house flies. The primary release point was a meat packing plant located on the north bank of the dry, barren Salt River bed. In a previous dispersion experiment, when this same release point was employed, it was demonstrated that the area immediately south of the release point was unattractive to flies (Schoof, *et al.*, 1952). Thus, for the purposes of the present study, the trap stations were confined to the zone north of the primary release point.

TABLE 1

Total flies released versus total flies recovered

SPECIES	RELEASED	RECOVERED	
		Radioactive[1]	Radioactive and dyed[2]
Musca domestica	147,186	6408	104
Callitroga macellaria	6,926	78	4
Phormia regina	3,463	41	5
Phaenicia spp.	13,852	736	42
Total	171,427	7263	155

[1] Exclusive of primary release site.
[2] Exclusive of secondary release sites.

TABLE 2

Rate of recovery of Musca domestica *and* Phaenicia *spp. in sectors I, II, III*

	SECTOR I	SECTOR II	SECTOR III
No. sites	14	21	13
Av. no. *Musca domestica*/site	68	58	109
Av. no. *Phaenicia* spp./site	10	18	15

Secondary release sites were chosen to represent locations which would depict contrasting dispersion of flies from that of the primary release point.

RESULTS

The rate of recovery of marked, undyed specimens far exceeded that manifested in previous studies despite the fact that no collections were effected prior to 48 hours after the initial release. As Table 1 indicates, a total of 6,408 radioactive house flies was retrieved in the 69 traps located at the 48 different sites.[3] This yield represents a recovery of 4.4 per cent of the house flies liberated. Only two of the 69 trap stations failed to show a radioactive specimen of *M. domestica*.

As the distribution of positive stations in Figure 1 reveals, the dispersion from the primary release point was essentially random in pattern. However, when the stations are grouped into three equal sectors and the data segregated (Table 2), it is evident that the greatest number of tagged specimens (109 per site) was captured in sector III. Consideration of the number of *Musca domestica* captured per site at 0.3, 0.5, 0.7, and 1.0 mile distance intervals demonstrates that the same held true for all intervals except at 0.5 mile. Approximately 52 per cent of the total tagged flies recaptured were taken within 0.5 mile of the primary release point.[4]

The recoveries of radioactive, colored flies are given in Table 3. The total of

[3] The release point trap is excluded and sites represented by more than one trap are counted only as a single site.

[4] The number of trap sites in the 0.5 to 1.0 mile zone was approximately three times that in the 0.0–0.5 mile band, this being in proportion to the areas of the two zones.

TABLE 3

Recovery of radioactive colored flies liberated at secondary release sites X, Y, and Z[a]

MILES	NO. OF SITES	NUMBER OF				
		Musca domestica	*Phaenicia* spp.	*Phormia regina*	*Callitroga macellaria*	Total
Site X						
.25	10 (2)[b]	15 (2)[c]	9 (3)[c]	2 (2)[c]	0	26 (7)[c]
.50	11	11	5	0	1	17
.75	16	3	1	1	0	5
1.00	10	0	0	0	0	0
1.25						
Total.....	47 (2)	29 (2)	15 (3)	3 (2)	1	48 (7)
Site Y						
.25	12 (2)	6 (25)	7 (4)	1	0	14 (29)
.50	20	25	6	0	0	31
.75	8	1	0	0	0	1
1.00	7	3	2	0	0	5
Total.....	47 (2)	35 (25)	15 (4)	1	0	51 (29)
Site Z						
.25	4 (1)	17 (1)	8	0	2	27 (1)
.50	10	9	0	1	0	10
.75	11	8	3	0	1	12
1.00	9	3	1	0	0	4
1.25	10	3	0	0	0	3
1.50	4	0	0	0	0	0
Total.....	48 (1)	40 (1)	12	1	3	56 (1)
Grand Total.....		104 (28)	42 (7)	5 (2)	4	155 (37)

[a] Since release sites extended over an area of 2 to 5 blocks, an arbitrary midpoint was selected for computing the distance intervals.

[b] Figures in ( ) represent stations at respective secondary release sites.

[c] Figures in ( ) represent flies captured at respective secondary release sites.

104 *M. domestica* retrieved from the three secondary release points represents a rate far in excess of that originally anticipated. Since it was not possible to determine the number of radioactive flies captured at each of the secondary release points without monitoring the specimens and possibly injuring them in the process, this number was estimated on the basis of data from previous dispersion studies. In a June, 1952, release of 70,000 house flies from the primary release point, an average of 7.5 flies per trap day was obtained in the 0.3 to 0.5 mile distance band for the first two days after release. By application of this index to the present test (147,186/70,000 × 7.5 × 90 trap days) it is estimated that approximately 1,418 dyed, radioactive *M. domestica* were placed in circulation

RECOVERY OF RADIOACTIVE DYED *Musca domestica* AND *Phaenicia spp.* LIBERATED AT SECONDARY RELEASE SITE "X"

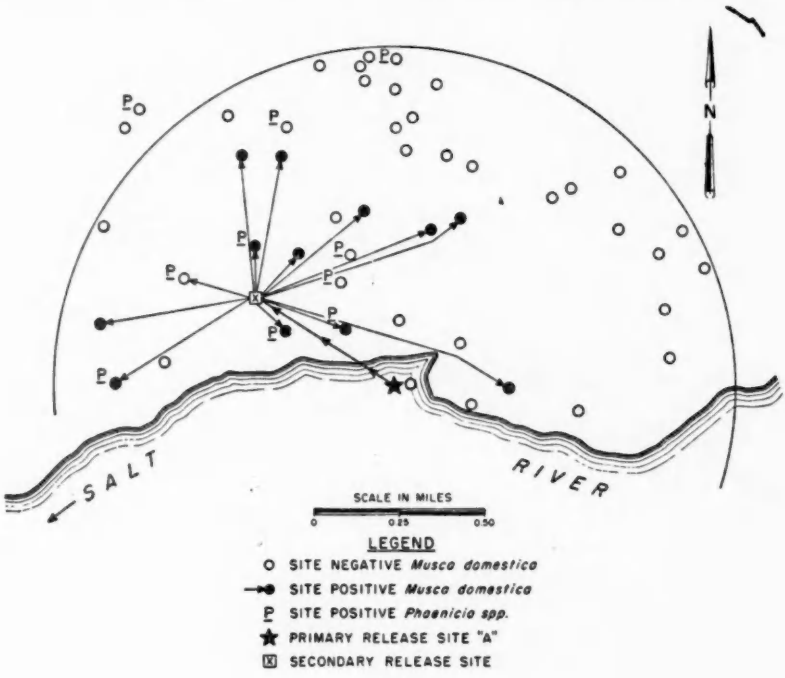

FIG. 2

at the three secondary release points. The 104 house flies retrieved thus would represent a recovery rate of 7.3 per cent, a rate which, while admittedly subject to latitude, is almost twice that for the flies recovered from the primary release site (4.4 per cent).

The movement of radioactive, dyed house flies from each of the secondary release sites is depicted in Figures 2, 3, and 4. As the radiating lines illustrate, *M. domestica* displayed a random dispersion from each secondary liberation site. Equally obvious was the reciprocal type of migration which characterized the movement of *Musca domestica*. Although in only one instance did a specimen return to the primary site of release, the examples of a reversal in directional movement were manifest. The recovery rates per distance intervals indicated that 65 to 89 per cent of the retrieved flies were captured within 0.5 mile of the release points. At the secondary release points, particularly site Y, radioactive colored flies were recovered as long as 5 to 7 days after their liberation.

While the objective of this test concerned the dispersion of *Musca domestica*, a sufficient number of tagged blow flies was recovered from the release at the pri-

RECOVERY OF RADIOACTIVE DYED *Musca domestica* AND *Phaenicia spp.* LIBERATED AT SECONDARY RELEASE SITE "Y"

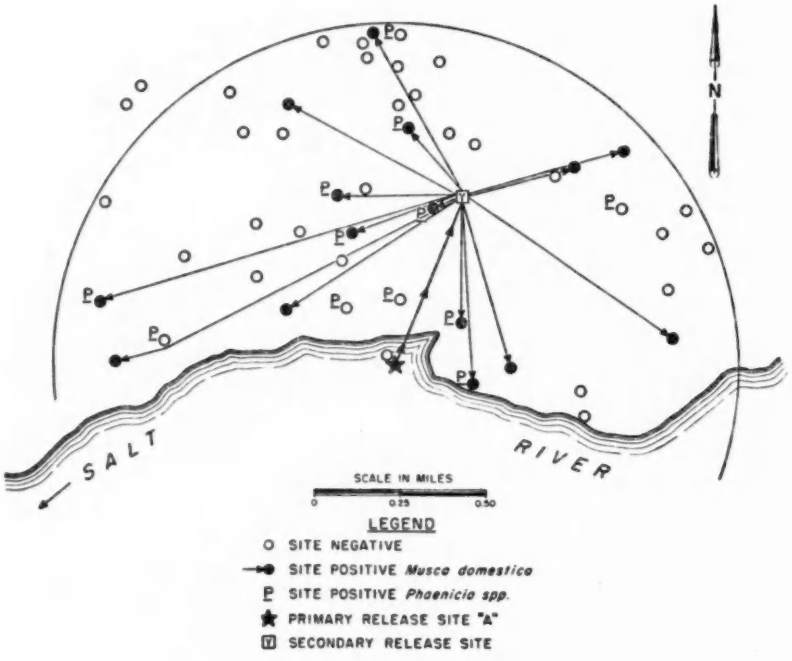

FIG. 3

mary liberation site to provide information on their dispersal habits (Table 1). The greenbottle flies, *Phaenicia* spp.[5], displayed the same type of random dispersion as *M. domestica*, this species being recovered from 63 of the 69 trap stations. The number of radioactive, colored *Phaenicia* recovered was only 42, but the distribution of sites positive for this species around each secondary release point exhibited a random pattern (Figures 2, 3, and 4). The highest recovery rate of *Phaenicia* in the three sectors was found in sector II. As with *Musca domestica*, the greatest percentage (56 per cent) of *Phaenicia* was taken within 0.5 mile of the release point.

The recapture pattern of *Callitroga macellaria* and *Phormia regina* followed the random design displayed by *Musca domestica* and *Phaenicia* spp. *Phormia regina* occurred in collections from 26 of the 69 trap stations; *Callitroga macellaria* from 36 trap stations. The recapture of dyed, radioactive specimens of both species was too meager to permit consideration.

During the test period from October 30 to November 10, maximum tempera-

[5] *Phaenicia sericata* and *Phaenicia pallescens*. Since the former constituted approximately 80 per cent of the *Phaenicia* recovered, the data pertain primarily to that species.

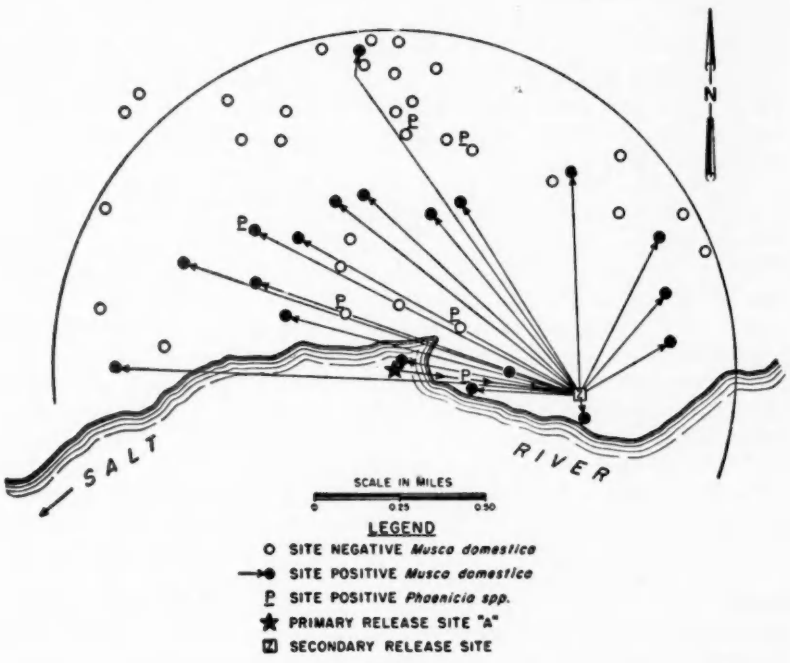

FIG. 4

tures averaged 81°F.; wind velocity 4.8 miles per hour, and minimum relative humidity 69 per cent.

DISCUSSION

The findings from these studies indicate that the house fly is essentially an insect of migrating habits as suggested by Parker (1916). The data reveal that although *Musca domestica* may aggregate in greater numbers at certain sites or localities, the majority of the individual specimens captured probably arrived at these destinations through devious routes of movement. Thus, the recovery of any single specimen at a particular site gives no clue as to the pattern of movement other than that the fly started its journey at one point and finished it at a second point. Even the collection of a large number of marked specimens at a release point over a period of several days is not proof that some of the recovered flies did not disperse from that point prior to their capture.

Essentially, the pattern of house fly dispersion initially involves a random movement from the point of origin until the insect reaches a site which provides the necessary stimuli for a temporary cessation of migration. When the stimuli

at this second site are modified or if the response behavior of the insect is altered, then dispersal of the fly again ensues in a random design. The same sequence of incitation and response occurs at each succeeding site until terminated by the death of the individual. However, since certain areas consistently offer favorable stimuli which incite the greatest responses from the flies and since the insects in their haphazard type of wandering sooner or later meander into these locations, it follows that such areas will be characterized by the maximum fly populations. Consequently, in dispersion studies, these same sites generally provide the maximum collections of tagged flies.

The significance of the roaming habits of the house fly in disease transmission is paramount. Obviously, by pausing at an undeterminable number of attractive sites (garbage, excrement, food, etc.), these flies have a far greater opportunity of distributing pathogenic organisms within an area than would be the case were their movements limited to a few locations. The fact that movement does occur from, as well as to, highly attractive areas, likewise augments their importance as a vehicle of disease dissemination. Thus, flies produced within city environs conceivably could migrate to sources of disease pathogens beyond urban limits and thereby become contaminated. In their subsequent circuitous movement, certain of these contaminated flies presumably would return to the community and, in this manner, would create a potential health hazard to the municipality.

From the control standpoint, the data are of value in appraising the importance of fly production sources beyond the boundaries of a community. The effect upon the community fly problem of a prodigious fly production site located one mile or more from the urban zone is governed by the characteristics of the area intermediate between the city and site. If this intervening zone is relatively devoid of attrahents and at the same time suitable attractants exist in the expanse beyond the problem fly-production source, fly movement away from rather than toward, the city is favored. If the opposite conditions prevail, migration towards the community is more likely to occur. However, when the latter results, the degree of population migration towards the community diminishes with each attractant visited because of the random type of movement which *Musca domestica* displays at each attrahent. Theoretically, at each attractant site, 50 per cent of the flies which egress from that point will move towards the town, and the balance will reverse towards the site of origin. Because of the reciprocal type of movement, the chances for house flies which develop at the problem source to infiltrate into the community itself may to a large extent dissipate in the intermediate zone. Were it not for the progressive decline in numbers caused by such a movement pattern, the effective range of migration of the mass population would probably be well beyond 1.0 mile.

Despite the fact that a relatively smaller number of migrants may reach the city environs, those that penetrate the intermediate zones may cause secondary effects by providing the "seed" for fly infestations within the zone. The resultant progeny in many instances would then be capable of invading the community proper.

In devising an approach to the problem of sites of copious fly production at or

beyond one mile, the control officer can focus his attention on controlling fly production either in the intermediate zone, at the problem fly-production source, or at both. While a fixed approach obviously cannot serve all situations of this type, the recommended course is to concentrate the abatement efforts within the intermediate zone. Such control tactics, by reducing the number of breeding and attractant sites, lessen the chances of fly infiltration from outlying areas and curtail the amount of fly production which can occur in the close proximity of the city.

In view of their propensity for haphazard movement, it is a matter of conjecture as to the total distances that house flies may travel. Nevertheless, since considerable movement to distances of one mile and individual sorties of 5 to 20 miles have been recorded for the species, it is not unreasonable to predict that house flies frequently may accumulate travel of 15 miles or more during the course of their existence.

SUMMARY

At Phoenix, Arizona, approximately 147,000 radioactive *Musca domestica* were liberated at a primary release site. For the 2-day period following, 15 fly traps were operated at 3 secondary sites 0.5 mile from the primary release point; the flies collected at each secondary site were then dusted with a characteristic dye, after which they were again liberated.

Collection stations within one mile of the primary release point indicated that, even though fly dispersion from that site followed a general random design, one sector of the recovery zone yielded a higher rate of recapture of radioactive specimens than the remaining sectors.

A total of 104 radioactive and dyed *M. domestica* was retrieved. Fly movement from each of the 3 secondary release sites exhibited a random pattern. Reciprocal migration was manifested, certain specimens reversing their initial path of migration and returning to the general area of the primary release site.

The data indicate *M. domestica* to be essentially an insect of migrating habits. The house fly apparently spends the greater part of its existence in moving from site to site not only in search of breeding and feeding sources but also from an inherent instinct to wander.

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MINUTES OF THE ANNUAL COUNCIL MEETING

The annual business meeting of the Officers and Councilors was held at The Brown Hotel. The meeting was called to order by the President, William A. Sodeman, on the evening of November 12. At adjournment, the agenda had not been completed, so that another meeting was held on the following day. Officers and Councilors present were: Frederick J. Brady, Lewis W. Hackett, Donald L. Augustine, Herbert G. Johnstone, Edwin H. Lennette, and G. Robert Coatney. Past-Presidents of the parent Societies in attendance were: E. Harold Hinman, George H. Bradley, Edward I. Salisbury, Paul F. Russell, and Hamilton H. Anderson. Dr. E. Harold Hinman represented the American Academy of Tropical Medicine.

The minutes of the first meeting held November 13, 1952 in Galveston, Texas were accepted as published in the May, 1953 issue of the JOURNAL.

The Secretary's report was presented as follows:

By permission of the Council, the past Secretary-Treasurer, Dr. Quentin M. Geiman, remained in office until December 31, 1952. Therefore, the present report covering the period from November 1, 1952 to October 31, 1953 includes activities during November and December of last year before the undersigned assumed office. Highlights of the year were: (1) receipt of the final decree of dissolution and the remaining assets of the American Society of Tropical Medicine, (2) enactment of a new three-year publishing agreement with the Williams & Wilkins Company, and (3) arrangements for the annual meeting. Other items of interest are included by number below.

(1) *Dissolution of the American Society of Tropical Medicine.* On April 9, the decree for the dissolution of the American Society of Tropical Medicine was lodged for record in the Pennsylvania courts. Following receipt of a certified copy of the final decree and the remaining cash assets (see Treasurer's Report below), negotiations were initiated with the Federal Reserve Bank of Richmond for reissue of the Government Bonds ($6,512.00 at cost) to our new Society. Although many months have passed since the application for reissue and evidence of ownership were submitted, at the time of writing the bonds have not been received from the Treasury Department.

(2) *New publishing agreement.* The present publishing agreement with the Williams and Wilkins Company was written to cover two years only, so that it could be re-examined after

a trial period. Since this agreement expires on December 31, 1953, consideration of a new agreement was necessary this year. Upon receipt in March of the 1952 financial statement for the JOURNAL showing a sizeable profit (see Treasurer's Report below), the Editor, Editorial Board, and the Officers and Councilors were requested to consider renewal of the present agreement. The response favored renewal, and while a few suggestions were made to improve the document, the replies indicated a high degree of satisfaction with our present agreement. Correspondence was then begun with the Williams and Wilkins Company, and a new three-year agreement was executed. While this agreement is similar to the present one, certain points have been spelled out for clarity. Our copy of the agreement is in the files of the Editor where it is available for reference purposes.

(3) *Annual meeting.* After the various committee members and representatives for the year had been notified of appointment by the President, and after other pressing matters were put in order, arrangements for the annual meeting were begun. In March, the Officers and Councilors gave approval to a request from the Academy to sponsor a symposium, and they selected the topic and moderator for our symposium. The announcement of the meeting, including a ballot and the annual call for papers, was mailed to each member on May 25th. From then until the time of the meeting, the necessary arrangements were made through correspondence with the local committee, and various other committees and individuals.

(4) *Letter to certain members of the parent societies.* Although last year all active members of the two parent Societies were notified about the formation of the new Society and were billed for dues in the new Society, it seemed desirable to recontact those who failed to respond. Accordingly, 56 members of the American Society of Tropical Medicine and 64 members of the National Malaria Society, all in good standing at the time the new Society was formed and thus eligible for transfer, were written a personal letter inviting them to join the ranks of the new Society. Of the 120 individuals written, thus far 16 (13.3 per cent) have become active members in the Society.

(5) *Membership.* As of October 31, 1953, the Society had 1090 active members in good standing. Thirty-five others who were in good standing last year failed to respond to statements of dues sent on three occasions. In addition to the active members, there are 16 honorary members and 4 emeritus members making a grand total of 1110 members.

Included in the above total of active members are 88 new members elected after publication of the 1952 transactions. The new members are as follows:

Adams, G.
Agosin, M.
Barber, I. W.
Baughn, C. O.
Berge, T. O.
Berry, M. G.
Blakeslee, T. E.
Bonnet, D. D.
Brandt, M. C.
Bras, G.
Buchman, E.
Burnham, K. D.
Campbell, C. H.
Coker, C. McL.
Comstock, E. G.
Contacos, P. G.
Cox, H. W.
Davenport, R. E.
Dern, R. J.
Derryberry, O. M.
Diaz-Rivera, R. S.
Dunne, T. B.
Elbel, R. E.
Friedl, F. E.
Galliard, H. L.
Gilani, A.
Goggin, L. M.
Greene, R. A.
Guijarro, A.
Gunther, C. E. M.
Haddon, W., Jr.
Harley, G. W.
Hathaway, J. S.
Hendricks, J. R.
Heyneman, D.
Hutchison, W. F.
Jung, R. C.
Kade, H.
Kilpatrick, J. W.
Kleinschmidt, R. E.

Kraus, H.
Lazarus, F.
Littig, K. S.
Loh, P.
McCarthy, D. A., Jr.
McDowell, J. W.
Maldonado, J. F.
Marin, J. D.
Markey, R. L.
Marques, R. J.
Moore, L. L. A., Jr.
Munch, J. C.
Myatt, A. V.
Natt, M. P.
Nowicki, E. L.
Oonyawongse, R.
Palmer, D. F.
Pan, C.
Pascuzzi, R. D.
Pimentel, D.
Pinckney, E. R.
Pradatsundarasar, A.
Rapalski, A. J.
Reihmer, V. A.
Rinehart, R. E.
Saleh, M.
Saylor, L. W.
Schoof, H. F.
Shaffer, J. G.
Shaheen, A.-S. F.
Simpson, T. W.
Singer, I.
Smith, E. M.
Tarizzo, M. L.
Teodorovic, S. D.
Thorson, R. E.
Tully, J. G., Jr.
Umanzio, C. B.
von Pohle, C. L.
Wainschel, J.
Walcott, A. M.
Wallis, R. C.
Weinstein, J.
Werner, C. A.
Wilks, N. E.
Winter, M. W.
Wolman, A.
Yaeger, R. G.

The Secretary announces with regret the loss by death of two honorary and five active members:

Barber, M. A., Honorary Member
Burke, A. W.
Cox, W. C.
Kelser, R. A.
Madwar, S. M.
Thurman, D. C., Jr.
White, J. H., Honorary Member, Past-President, 1911–1912.

The following 29 members submitted resignations:

Abramson, W.
Allison, T. D.
Cass, J. S.
Chappell, R.
Clowes, G. H. A.
Cole, B. A.
Dill, D. B.
Frazier, C. N.
Gamache, E. F.
Harrell, G. T.
Herndon, H. V.
Howard, W. A.
Jameison, W. A.
Jensen, J. R.
Johnson, H. F.
Johnson, H. A.
Keener, G. G., Jr.
Legwen, W. A.
Lenke, S. E.
Lenert, L. G.
Matheson, R.
Meranze, D. R.
Mustard, H. S.
Rector, N. H.
Redmond, W. B.
Sanders, J. P.
Schwartz, S. C.
Stone, W. S.
White, C. M.

(6) *Letters to the Officers and Councilors.* Four letters were mailed during the year for expression of opinion and vote. On March 10, a letter was sent giving a statement of the status of Society business in the office of the Secretary-Treasurer, and items relating to the annual meeting were submitted for vote. The results, based on a majority vote, were as follows: (1)

the Academy's request to sponsor a symposium at the Louisville meetings was granted, and (2) it was voted that the Society sponsor one symposium this year, that the topic be, "Diarrheal Diseases other than Amebiasis", and that Dr. James Watt be requested to serve as moderator. On April 20, the Officers and Councilors were asked to vote on the dates of our Louisville meetings, since the dates selected originally (November 12–14) were found to conflict with the A.P.H.A. meetings, and a new publishing agreement was submitted for suggestions and vote. The majority voted in favor of retaining the dates of November 12–14 for our meeting, and the publishing agreement was approved unanimously. On July 18, the following items were submitted to the Officers and Councilors for consideration and vote: (1) The Committee's nomination of Dr. L. W. Hackett for the Walter Reed Medal (a favorable vote of two-thirds of the Officers and Councilors is required for selection of the recipient), (2) The Anniversary Committee's request for funds to purchase 100 medals commemorating the 50th anniversary of the founding of the American Society of Tropical Medicine, (3) time of the Council meeting at Louisville, and (4) approval of the dates of November 4–6 for our 1954 meetings. Dr. Hackett's nomination for the Walter Reed Medal was approved unanimously, and the Anniversary Committee was authorized to spend $465.00 for 100 commemorative medals. It was voted to hold our Council meeting after the celebration dinner on Thursday, November 12th, and the dates of November 4–6 for the 1954 meetings were approved unanimously. A final letter was sent to the Officers and Councilors on October 19th concerning plans for the annual meeting and an invitation to attend the meeting and submit items for Council consideration.

Other activities. Those in connection with various committees will be presented below under the appropriate headings.

Finally, the fine cooperation of the Officers, Councilors, Committees and other members in transacting the business of the Society is hereby acknowledged with sincere thanks and appreciation.

Respectfully submitted,
JOHN E. LARSH, JR.
Secretary

The report of the Secretary was accepted as read.

The report of the Editor of the AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE was presented as follows:

Our JOURNAL is now well along in its second year of life and seems to be in excellent shape both financially and in the number and quality of the contributed papers. Complete figures and statistics are available only for Volume I (1952) and the financial report for that year, prepared from data supplied by the publishers, is presented in Table 1. With it, for comparison, are given the figures for Volume 31 which closed the file of the AMERICAN JOURNAL OF TROPICAL MEDICINE in 1951.

The increase in income from subscriptions, extra pages purchased by authors, and advertising was greater than the increase in production costs, in spite of the growth in size of the JOURNAL. The printing cost per page of text went down slightly, in fact, from $12.86 in 1951 to $12.35 in 1952, the first decrease in many years, and the other comparative figures are also encouraging.

Increase in income	35.0%
Increase in production cost	17.4%
Increase in circulation	7.2%
Increase in number of pages of text	21.8%
Increase in pages of advertising	153.6%

Authors or their institutions defrayed the cost of printing 244 extra pages, or about 23 per cent of the total pages of text published. This is about what we should try for. The

TABLE 1

Financial statement for Volume 31, American Journal of Tropical Medicine and for Volume 1, American Journal of Tropical Medicine and Hygiene

	VOL. 31 (1951)	VOL. 1 (1952)
Income:		
Paid subscriptions	$11,440.50	$18,604.00
Less credit for unusued pages transfered to reserve*	0.00	1,488.32
Total available from subscriptions	11,440.50	17,115.68
Net profit from advertising	309.13	2,417.06
Paid by authors for extra pages	2,738.09	3,339.78
Net from reprint sales	558.51	72.45
Back volume sales	491.31	425.44
130 excess pages @ $13.63 paid by Am. Soc. Trop. Med.	1,771.90	0.00
Total income	17,309.44	23,370.41
Production cost:		
Manufacturing	11,317.60	13,241.15
Distribution, overhead, etc.	2,975.42	4,068.72
Total costs	14,293.02	17,309.87
Surplus:	3,016.42	6,060.54
Accruing to Am. Soc. Trop. Med. (50%)	1,508.21	3,030.27
Circulation and size:		
Paid subscriptions—members	847	1,071
nonmembers	1,347	1,282
Total subscriptions	2,194	2,353
Pages, text	880	1,072
Advertisements	57	144
Total pages	937	1,216

* 72 pages in 1952.

number of manuscripts submitted for publication varies greatly from month to month, but if the present rate is maintained, we should try to keep the size of each issue at about 200 pages, as has been the case for the last four numbers (including November). Since the publisher guarantees 150 pages, the additional 50 pages, or 25% of the text, must be financed from subventions by authors or paid for out of the surplus refunded by the publishers. This amounted to $3,030.27 in 1952, more than double that of the year before. In 1952, however, the influx of acceptable manuscripts did not keep pace with the projected expansion of the JOURNAL, so that we fell 72 pages behind our available total in the course of the year. These unused pages remain to our credit with the publishers and can be utilized at will. We also have a balance in the JOURNAL account of some $2,000, provided in previous years for extra pages, which it has not been necessary to draw upon. We are in a position therefore financially to put manuscripts into circulation at the rate of 200 pages an issue if the supply is sufficient, and at the present time it is abundantly so.

Our aim will be to keep the backlog of papers at a comfortable level which would permit publication of papers within 6 to 8 months of their reception and at the same time provide

TABLE 2

Number and disposal of manuscripts submitted

MANUSCRIPTS	VOL. 31 (1951)		VOL. 1 (1952)	
From previous year		58		65
Submitted during year	143		148	
Declined	27		23	
Withdrawn	8		9	
Accepted		108		116
Available for publication		166		181
Published during year		101		118
On hand for next volume		65		63

TABLE 3

Subjects and approach of papers published by the Journal in 1952 and 1953

SUBJECT	1952	1953	APPROACH	1952	1953
Animal hosts and vectors	23	23	Biology and taxonomy	9	9
Bacteria and fungi	7	9	Clinical (diagnosis & treatment)	28	31
Deficiencies and nutrition	0	0	Epidemiology and statistics	28	23
Helminths	17	16	Experimental—field	5	5
Protozoa	49	50	Experimental—laboratory	28	30
Viruses and rickettsias	18	7	Prevention and control	14	11
General and miscellaneous	4	7	Others	6	3
Total	118	112	Total	118	112

the Editor with an inventory always sufficient for at least three complete issues. The status of the manuscripts submitted for publication in 1952 as compared with 1951 is shown in Table 2.

The fields covered by these papers and the type of approach selected to achieve the reported results are shown in Table 3. Since the November issue for this year is already made up though not in print, the figures for 1953 can also be shown. Some papers are concerned with several fields and more than one approach, and the classification in such cases is therefore somewhat arbitrary.

It seems to the Editor extraordinary that such a relatively small number of papers from so many different sources should follow the same pattern so exactly from year to year both as to subject and approach. It is dismaying to find that deficiency diseases and nutrition, subjects so important in tropical medicine and hygiene, are not being treated at all in our JOURNAL. It is likely that much is being done in this field, but that the reports appear in more specialized periodicals. Table 3 also raises the question as to whether the fairly stable sources of funds for research, whether from government, industry or foundations, may not influence the pattern of investigation. An analysis has been made of the type of sponsorship of the last 200 papers published in our JOURNAL, and this is shown in Table 4.

It appears from this table that about 60% of the work reported in our JOURNAL during 1952 and 1953 was financed by U. S. Government funds, 26% by private agencies in the

TABLE 4

Scientific sponsorship and source of funds of work reported in the Journal, January, 1952–September, 1953

AGENCY	SCIENTIFIC PROJECTS			
	Executed*		Subsidized*	
	Number	Per cent	Number	Per cent
Federal Government				
P.H.S.—National Insts. of Health	31	15.5	47	23.5
—Communicable Disease Center	18	9.0	20	10.0
Army	11	5.5	17.5	8.7
Navy	4	2.0	13.5	6.8
Veterans Administration	3	1.5	3	1.5
Gorgas Memorial Laboratory	7	3.5	7	3.5
Other Fed. Agencies, work in U.S.A.	2	1.0	2	1.0
Other Fed. Agencies, for work abroad	—	—	4.5	2.3
Subtotals	76	(38.0)	114.5	(57.3)
State and Local Agencies	6		4.5	
Subtotals	6	(3.0)	4.5	(2.2)
Private Agencies				
Universities	50.5	25.3	30	15.0
Hospital, Clinics and Labs	5.5	2.7	4	2.0
Foundations	4	2.0	7	3.5
Industry	8	4.0	11	5.5
Subtotals	68	(34.0)	52	(26.0)
Work Done Abroad				
By Americans	23	11.5	2†	1.0
By Nationals	27	13.5	27	13.5
Subtotals	50	(25.0)	29	(14.5)
Total Projects	200	100	200	100

* Projects jointly executed or subsidized are proportionately credited.

† Financed abroad.

United States, and 14% by nationals of foreign countries. If we restrict the inquiry to the United States by omitting the foreign papers, the percentages are altered as follows:

Source of funds	*No. of papers*	*Per cent of total*
Government funds	119	70
Universities, hospitals, private labs., etc.	34	20
Industry	11	6
Foundations	7	4
	171	100

According to *Science* (Sept. 25, 1953) the 181 million dollars spent on medical research in the United States in 1951 was provided as follows: Federal Government, 42%; Industry, 33%; and other sources, 25%.

Our field is of course a special one, with its own peculiar distribution. Industry plays a much greater role in medical research in the United States, and hospitals and medical schools a lesser one than would appear from our small sample. However, it does point up the impression which is fairly general that American industry and trade are not supporting research in tropical medicine to an extent commensurate with their financial interest in the tropics. Whether there is any tendency for extra-mural sponsorship of medical research to regiment investigation or direct it at selected targets and thus diminish so-called pure or basic research cannot be deduced from these figures.

Respectfully submitted,
L. W. HACKETT
Editor

The Editor's report was accepted as read.

The report of the Editor of TROPICAL MEDICINE AND HYGIENE NEWS was presented as follows:

The mailing list of the TROPICAL MEDICINE AND HYGIENE NEWS remained approximately the same during 1953. There was a slight diminution due to a reduction in the list distributed for the American Foundation for Tropical Medicine, but this was almost made up by some gain in circulation to our own list.

We are greatly indebted to our advertisers, Burroughs Wellcome and Co., Merck and Co., Charles Pfizer and Co., and Winthrop-Stearns Inc. for their financial support. Also, thanks are due to the American Foundation for Tropical Medicine Inc. which has borne part of the cost of printing and mailing in return for distribution of the NEWS to its mailing list.

A considerable change in the production of the NEWS was made at the start of 1953. The printing is now done by the photo offset process, with copy preparation by means of IBM proportional spacing machines. The change was initiated for two reasons: first, the production of the NEWS on schedule was always a problem when the bulletin was printed by the plate printing technique in Baltimore; because of the nature of the material in this publication a long delay between copy preparation and appearance of an issue detracted from its effectiveness. Secondly, at the start of the year our economic outlook was not bright due to the withdrawal of two advertisers, and it appeared feasible to cut production costs by the new technique. After the change was made we were fortunate in obtaining the patronage of a new advertiser, but nevertheless our total advertising revenue for the year was reduced. Despite the loss of revenue, the economy measures resulted in some gain in our financial position.

In general, such comments as we have received have reflected no dissatisfaction with the appearance of the NEWS as produced by the new method. However, there has been one very definite complaint that the bulletin does not appear as well printed as by the old method. It is hoped that more members of the Society will express themselves on this matter.

An additional printing of 5,000 copies of "Health Hints for the Tropics" was made during the year. Of these, the American Foundation for Tropical Medicine ordered 2,500 for distribution to business firms, and we purchased the rest because of the diminished supply and continuing demand. The cost of this printing has already been paid by receipts from sales of the supplement.

There has been a very gratifying increase in the number of news items and reports which we have received from Society members. We are grateful to the members who have sent us

newsworthy items and we wish to encourage all members to let us know of their activities and of special events with which they are familiar.

Respectfully submitted,
LEON JACOBS
Editor

FINANCIAL STATEMENT

Tropical Medicine and Hygiene News

November 12, 1952 to November 12, 1953

Balance in bank, November 12, 1952	$1760.83
Deposits:	
Advertising receipts	2375.00
American Foundation for Tropical Medicine	383.25
Sale of supplements	1224.42
Sale of reprints	19.00
Total receipts	$5762.50
Disbursements:	
Payment to Society, December, 1952	$1000.00
Copy preparation	469.55
Printing and preparing for mailing	1235.52
Deposits for permit postage	140.00
Envelopes	212.05
Stamps (including foreign postage on NEWS) and miscellaneous office expenses	119.79
Reprinting of 5000 "Health Hints"	274.50
Total disbursements	$3451.41
Balance in bank, November 12, 1953	$2311.09
Assets, November 12, 1953:	
Bank balance	$2311.09
Accounts receivable:	
Advertising	375.00
Amer. Found. Trop. Med.	90.16
Sales of "Hints"	39.00
Deposit for permit mail	22.58
Petty cash	3.71
Total assets	$2841.54
Total liabilities, November 12, 1953	0000.00
Net worth	$2841.54

The Council voted to accept the report as read, and directed the Treasurer hereafter to list the assets of the NEWS in the Treasurer's report. The Editor was requested to state the need for secretarial assistance in his office, but action was deferred pending the report of the Finance Committee (see below).

The Treasurer's report was presented as follows:

The American Society of Tropical Medicine and Hygiene
Balance Sheet
October 31, 1953
Assets

Cash on hand		$15.31
Cash in bank		7,302.26
U. S. Savings Bonds, at cost:		
Series J	$2,016.00	
Series K	4,000.00	6,016.00
Total Assets		$13,333.57

Net Worth

Appropriated surplus:	
The American Journal of Tropical Medicine and Hygiene for extra pages	1,000.00
Unappropriated surplus	12,333.57*
Total Net Worth	$13,333.57

* Includes $2,247.76 transferred from the American Society of Tropical Medicine upon completion of liquidation proceeding in the Pennsylvania courts.

The American Society of Tropical Medicine and Hygiene
Statement of Receipts and Disbursements
Year Ended October 31, 1953

Balances, November 1, 1952:		
Cash on hand		$19.41
Cash in bank		7,555.08
Total		$7,574.49
Receipts:		
1953 membership dues, net of refunds	$9,106.91	
1954 membership dues, net of refunds	3,890.65	
Profit on Journal for year 1952	3,030.27	
Cash transferred from The American Society of Tropical Medicine, in liquidation	2,247.76	
Publication of Tropical Medicine and Hygiene News	1,000.00	
Registrations, et cetera, from annual meeting in Galveston, Texas	537.19	
Contributions for 1953 annual meeting	400.00	
Share of income from commercial exhibits, Galveston, Texas, meeting	334.64	
Commemorative medal sales	107.25	
Interest on U. S. Savings Bonds	55.20	
Sales of back issues of Journal of The National Malaria Society	7.00	20,716.87
Total		28,291.36
Disbursements:		
Subscriptions to the Journal	9,912.00	
Secretarial assistance	1,370.00	

Bailey K. Ashford Award	1,150.00	
Convention and travel expenses	741.18	
Printing, stationery, and office supplies	699.13	
Reprints and printing costs in Journal paid with funds transferred from The National Malaria Society	615.69	
Advances to 1953 local committee	500.00	
Editorial office expense	492.85	
Commemorative medals	465.00	
Stamps, postage, and express	389.75	
Legal and auditing services	230.00	
Freight	200.52	
Fidelity bond of Secretary-Treasurer	93.75	
Corporate registration and filing fees	30.00	
Contribution to National Society of Medical Research	25.00	
Telephone and telegraph	24.52	
Walter Reed Medal	17.68	
Miscellaneous expenses	16.72	
Purchase of U. S. Savings Bonds—Series K	4,000.00	20,973.79
Balance, October 31, 1953		$7,317.57
Consisting of:		
Cash on hand		$15.31
Cash in Bank of Chapel Hill, Chapel Hill, N. C.		7,302.26
		$7,317.57

As directed by Council action at the Galveston meeting, $4,000.00 of Society funds were invested in U. S. Bonds (Series K—2.75 per cent interest). Despite this large disbursement item, we managed to keep the total receipts for the year ($20,716.87) within near balance with the total disbursements for the year ($20,973.79). This was made possible by the $3,030.27 profit on the JOURNAL for 1952, and the $1,000.00 transferred from the NEWS account. From a study of the financial status of the Society after two years of existence, it seems safe to conclude:

(1) that the present $8.00 rate for dues is satisfactory, and

(2) *that care must be exercised in commiting ourselves to any permanent financial obligations.*

Since it is now clear that our yearly surplus, if any, will depend on the profits from the JOURNAL and the NEWS, it would seem wise to consider on a year-to-year basis any future project(s) calling for a sizeable financial outlay.

Respectfully submitted,
JOHN E. LARSH, JR.
Treasurer

The Treasurer's report was accepted as presented. Discussion led to agreement on two points: one, that the surplus, if any, of the paper by Dobrovolny *et al.* (September, 1953 issue of the JOURNAL), which was subventioned by The Pan American Sanitary Bureau, be sent to the Treasury of the United States; two, that there is now a total sum of $2,000.00 in the Society Treasury for use by the Editor for extra papers in the JOURNAL.

Report of the Auditors: "Appointed by the President of the Society, we have examined the accounts of the Secretary-Treasurer of the Society and of the Editor of TROPICAL MEDICINE AND HYGIENE NEWS.

We had before us the report of the Certified Public Accountant for the records of the American Society of Tropical Medicine and Hygiene covering the period ending October 31, 1953, and the ledger of the Society. We find that the audit of the C.P.A. indicates the financial position of the Society to be that shown in the report of the Secretary-Treasurer.

We have examined the ledger, invoices and bank statements through November 12, 1953, of the TROPICAL MEDICINE AND HYGIENE NEWS. We find these accounts in order. No evidence of irregularity was found."

Respectfully submitted,
PAUL E. THOMPSON
WILLIAM G. SAWITZ

The report was accepted by the Council.

Reports of Committees

Academy Liaison Committee. Submitted by Albert B. Sabin

The Academy Liaison Committee, consisting of Doctors W. Clark Cooper, Archie D. Hess, Donald B. McMullen, Thomas H. Weller and the undersigned chairman, all of them nonmembers of the American Academy of Tropical Medicine, received the following charge from the President:

1. Explore relationship of the Academy to the Society in the annual meeting.
2. Confer with a similar committee of the Academy regarding the desires of the Academy and report back the majority and minority opinions of our committee on the proposals of the Academy.
3. Cooperate with the Academy's "Committee on the Future of the American Academy of Tropical Medicine" in "exploring the field of future activities of the Academy".

This report is based on correspondence and personal conversations between the chairman and the members of this committee as well as with the President and Secretary of the Academy and with the chairman of the "Committee on the Future of the Academy". There was no opportunity for a joint discussion prior to the annual meeting in Louisville.

Relationship of the Academy to the Society in the annual meeting. It must, first of all, be said that this committee looks upon the American Academy of Tropical Medicine as consisting of specially honored and eminent members of the Society of Tropical Medicine and Hygiene. There is no question here of the importance to the success of the annual meetings of the continued participation of these members as *individuals*. Almost all members of this committee, however, are aware of opposition on the part of many members of the Society to participation of the Academy in an official capacity as a distinct group or body. Four of the five members of this committee are against official participation of the Academy in the annual scientific program, and the fifth is indifferent. The reasons given are that the program is better planned and coordinated when a single group is responsible, that scientific symposia are better integrated into the general program by the regular program committee, and that symposia on general problems and aspects of tropical medicine and hygiene, while of interest and importance on occasion, can hardly become annual events.

We have received no proposals from the Academy regarding their own desires, because they are still struggling with the more fundamental question of "to be or not to be".

General aspects of the relationship between the Society and the Academy. Unless the Academy can embark on an active program under which it would function as a "general staff" for the planning and coordination of American work in tropical medicine and hygiene, obtain funds to further research and training in this field beyond the currently available short-term project grants, and cooperate with other national and international agencies interested in the development of the tropics for the benefit of all mankind, this committee sees no good reason for its existence as a separate body. Membership in the Society is based on mere interest in one or another phase of tropical medicine and hygiene, while membership in the Academy recognizes special achievement in this field. The majority of this committee

is in favor of amalgamating the Academy with the Society, converting the present members of the Academy into Fellows of the Society, and electing new Fellows in recognition of important contributions by younger members of the Society. This committee is influenced in its decision by the fact that 51 of 61 members of the Academy who were polled in 1952 favored either amalgamation with the Society or complete dissolution of the Academy. The "general staff", to be charged with furthering the interests of tropical medicine and hygiene in the U.S.A. and the world, could be organized and recruited under the auspices of the entire American Society of Tropical Medicine and Hygiene as well as, if not better than, under only a portion of its membership designated as the American Academy of Tropical Medicine.

Anniversary Committee. Submitted by Lewis W. Hackett

The Committee decided that the celebration should take the form of a dinner, at which as many as possible of the early Presidents of the Society would be asked to speak in a reminiscent vein. Invitations were sent to the first eight of the living ex-Presidents, of whom five accepted. Dr. Quentin Geiman was asked to prepare a paper based on minutes of the earliest meetings and other historical material. This will serve as a basis for a short talk at the dinner and will be printed *in toto* in the JOURNAL. The President of the Society, Dr. William A. Sodeman, will close the exercises by presenting the incoming President to the gathering.

The Officers and Council approved striking a commemorative bronze medal bearing the seal of the present Society on the obverse, and a suitable inscription referring to the 50th anniversary of the parent society on the reverse. This will be on sale to members at a modest price, the cost of the dies being provided from other funds.

Secretaries of foreign Societies of Tropical Medicine were apprised of the anniversary celebration and were informed that the Society would be pleased to have any of their members who might be in the United States at that time attend our scientific sessions and the anniversary dinner.

C. F. Craig Lectureship Committee. Submitted by Louis L. Williams, Jr.

The Chairman reported the unanimous choice of Dr. Henry E. Meleney to deliver the eighteenth annual Charles Franklin Craig Lecture.

Finance Committee. Submitted by Albert B. Sabin

The finance committee, composed of Doctors Hamilton Anderson, Edward I. Salisbury and the undersigned chairman, was directed to examine the Society's finances and to make recommendations on two specific points: 1) use of the surplus, and 2) the feasibility of a permanent secretarial office.

The present report is based on an exchange of views between the chairman and the members of the committee, and on information received from Dr. L. W. Hackett, in his capacity as Editor of the AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE, and from Doctors John E. Larsh, Jr. and Quentin M. Geiman, in their capacities as present and past Secretary-Treasurer.

Size of surplus. At the time of the annual meeting in November, 1953, the Society was found to have a surplus of $19,845.57 of which $12,528.00 is now invested in U. S. bonds paying less than 3% interest. This, however, does not include the sum of approximately $2,841.00 which are the assets of TROPICAL MEDICINE AND HYGIENE NEWS, which is now in custody of the Editor, Dr. Leon Jacobs. *The total surplus of the society is therefore approximately $22,686.00.*

Estimates of future income. The current annual surplus is derived almost entirely from the JOURNAL, and depends in large measure on the Editor's ability to charge authors for space in excess of 10 pages or in certain instances for the entire cost of printing. Continuation of this practice as well as continued income from advertising might be expected to yield an annual surplus of $3,500.00 or more.

Question of a permanent secretarial office. Members of the Society, who are noble enough to accept the job of Secretary-Treasurer, are active investigators and teachers and an inordinate amount of their valuable time is consumed by routine duties which are a part of this office. The following time-consuming activities of the Secretary-Treasurer's office could be carried on by an efficient nonprofessional person:

1) Maintenance of the membership file of the Society.
2) Maintenance of the non-member file receiving the NEWS and addressing of envelopes for mailing the NEWS.
3) Processing of subscriptions for the JOURNAL.
4) Issuance of bills and collection of dues.
5) Call for papers.
6) Maintenance of the files and archives of the Society.

The person elected as Secretary-Treasurer would then act with the other officers of the Society on matters of policy and would sign the checks.

Recommendations for use of currently available surplus. The committee was unanimous in its belief that the principal sum of the surplus should not be reduced too drastically and that all funds not needed for current operating expenses be invested in reliable bonds to yield at least 3% interest per annum. The committee was furthermore unanimous in the opinion that the annual interest from the investment, as well as a portion of the principal, be used for some purpose that would help to fulfill the objectives of the Society. Many members of the Society have expressed a wish to have invited, comprehensive reviews published in the AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE to help them keep abreast of the current status or recent developments in the varied fields which comprise tropical medicine and hygiene. Dr. Hackett has informed me that it would cost about $500.00 to print a review of 33 printed pages. If $20,000.00 of our estimated surplus of $22,686.00 were invested to pay a minimum of 3% interest per annum, we could expect an annual income of at least $600.00.

Recommendations.

1) Relief for the office of Secretary-Treasurer should be provided in two steps:
   a) Immediate increase in appropriation for secretarial help to the present Secretary-Treasurer.
   b) Exploration of the best way of establishing a permanent, nonprofessional Secretary-Treasurer's office to handle the nonprofessional business of the Society.
2) The present surplus of the Society should be handled in the following manner:
   a) Excepting funds required for operating expenses, invest all other funds in reliable bonds paying 3% or more interest per annum. This would mean that the $12,528.00 presently invested in United States bonds would be sold and reinvested in accord with the best financial advice that the Secretary-Treasurer may obtain. The Officers and Council of the Society should be informed by mail of the recommendations of the financial advisors and should then notify the Secretary-Treasurer of approval or disapproval.
   b) Use the interest and enough of the principal to pay for two or three comprehensive reviews to be published each year as part of the AMERICAN JOURNAL of TROPICAL MEDICINE AND HYGIENE.

If these recommendations are adopted, it is suggested that the Editor be requested to appoint a special committee to select both the subjects for review and the reviewers. If this project should work well during a period of two years, the Council should reconsider this matter and decide whether or not more reviews should be published annually and more of the principal expended for this purpose.

The Council approved the report as read. As a result of the Committee's recommendations to provide relief for the office of Secretary-Treasurer, the following actions were taken. The Secretary-Treasurer was authorized to spend

during the next year $200.00 monthly for secretarial assistance, and he was authorized immediately to purchase office equipment not in excess of $500.00, and the President was directed to appoint a committee to consider means by which the nonprofessional business of the Society can be handled in the future. There evolved from the discussion of secretarial assistance a motion to authorize the expenditure of not more than $600.00 per annum for this purpose by the Editor of TROPICAL MEDICINE AND HYGIENE NEWS. This motion was given favorable action.

As a result of the Committee's recommendations concerning the use of the surplus funds of the Society, the Secretary-Treasurer was instructed to carry out the suggestions of the Committee in regard to the investment of funds (2, a, above). It was also voted that the number of reviews to be published annually and the procedures for selecting subjects and reviewers be left to the judgment of the Editor and Editorial Board.

Membership Committee. Submitted by Harry Most

At the time of last year's meeting, 17 membership applications were pending. Last year's committee accepted 15 of these and rejected two. The present committee reviewed and approved 73 applications. Thus, a total of 88 new members have been added to our rolls during the past 12 months. In addition, 10 applications are pending. Total membership, not including the 10 applications pending, but including honorary and emeritus members as well as active members is 1110.

Honorary Membership Committee. Submitted by E. Harold Hinman

We believe that Dr. Henry Galliard, Professor of Parasitology at the University of Paris, School of Medicine, is an excellent candidate, and we recommend him for Council consideration.

The Council voted unanimously that Professeur Henri Lucien Galliard be elected an honorary member of the Society.

Program Committee. Submitted by John E. Larsh, Jr.

As mentioned in the Secretary's report, the Officers and Councilors voted on the title and moderator for our symposium, and the preferences were endorsed by the Committee. Soon thereafter, the Committee agreed by correspondence on a policy to follow this year in accepting papers for the scientific programs.

In response to the call for papers, 56 applications were received. The Committee selected 47 of these to be read, and the remainder were placed in the category, "To be read if time permits". In an effort to make space for the greatest number of papers without reducing greatly the time requested for presentation, the Committee voted to limit all papers to 10 minutes.

Committee on Teaching and Research in Tropical Medicine and Hygiene. Submitted by William W. Frye per Henry E. Meleney

The Microbiology (Tropical Diseases) Study Section of the National Institutes of Health at its meeting in May, 1953, authorized Dr. Frye to make a survey of medical schools to ascertain the status of teaching of tropical medicine at the present time. Dr. Frye expects to carry out such a survey during the next year.

He also reports that the National Microbiological Institute cannot at present grant

travel and training fellowships to study tropical diseases abroad. He thinks this would be desirable.

Walter Reed Medal Committee. Submitted by James S. Simmons

The Committee voted unanimously in favor of Dr. Lewis W. Hackett as the nominee for this award. Prior to the meeting, the Council voted unanimously to accept this nomination, thereby satisfying the condition of the award that the nominee be approved by a two-thirds vote of the Council.

The above reports were accepted as read.

Reports of Representatives to Organizations

National Research Council. Submitted by Harry Most

The annual meeting of the Division of Medical Sciences of the National Research Council was held on May 23rd, 1953 in Washington, D. C. The principal matter presented at this meeting which is of interest to the American Society of Tropical Medicine and Hygiene is contained in the report of the Sub-Committee on Malaria. The following statement is from the report of the Sub-Committee.

"The Subcommittee on Malaria believes that its mission, so imperative during and immediately after the war, is now approaching completion. The management of acute malaria with drugs presently available is well controlled and has ceased to be an urgent national problem. A large, intensive chemotherapeutic program is no longer justified.

Recent effort has concentrated on an examination of the suppressive action of the new drug, pyrimethamine, and on the determination of the best mode of combined therapy of malaria with chloroquine and primaquine. A highly successful 14-day regimen of combined treatment with chloroquine and primaquine, applicable on shipboard, has been developed and published as an editorial in the Journal of the American Medical Association (23 August, 1952).

As an antimalarial suppressant, but not as a therapeutic agent for management of malarial attack, pyrimethamine has held the major interest. Despite indications of serious toxicity to cynomolgus monkeys, tolerance of humans seemed adequate, and the drug's cheapness and availability recommended it.

Suppressive action of pyrimethamine, even in minute doses, against Chesson strain *vivax* malaria without previous experience of the drug was found excellent, and apparent suppressive cures were noted. Recently, the ready induction of drug fastness in this strain has been established. Resistance of numerous Paludrine-fast strains of *P. falciparum* to pyrimethamine has been reported. Thus the early promise of wide applicability of this drug as a suppressant for all types of malaria has not been upheld. Nonetheless, the indication of suppressive cures by pyrimethamine at a weekly level of 25 mg. continued over four months has been of sufficient interest to make further investigation desirable.

A large-scale military field test of the suppressive action of pyrimethamine was planned for Korea, but was abandoned because of administrative difficulties. Less extensive but more rigorously controlled studies in the United States will be undertaken."

Nominating Committee, Kimble Methodology Research Award. Submitted by Ernest Carroll Faust

The Nominating Committee presented to the Research Award Committee two nominees, both of whom are members of our Society. The announcement of the recipient will be made at the A.P.H.A. meeting shortly before we convene in Louisville.

Steering Committee, proposed American Board of Medical Microbiology. Submitted by Willard H. Wright

Following last year's meeting of the Society, the resolution voted by the Society was prepared and signed by the President, W. A. Sodeman, and the Secretary-Treasurer, J. E. Larsh, Jr. This was transmitted to Dr. Lowell T. Coggeshall, who represented the Society at the meeting with the American Medical Association in Chicago on February 5, 1953 in my absence in Liberia. At the request of Dr. Syverton, Chairman of the Steering Committee for A.B.M.M., I requested Dr. Norman Topping, Vice President of the University of Pennsylvania, to address a letter to Dr. Donald Anderson of the A.M.A. supporting the formation of the proposed Board. With the information at hand, there are no definite developments to report from the meeting of February 5 and later conferences held by various groups concerned with this matter.

Organizing Committee, International Society of Tropical Medicine. Paul F. Russell —no report, see following report.

Fifth International Congresses on Tropical Medicine and Malaria. Submitted by Martin D. Young

The main matters of interest to the members of our Society are embodied in a set of resolutions, which were passed on the last day. An Interim Committee was established with members distributed geographically as follows: Africa (2), South Africa (1), North and Central America (2), South America (2), Asia (4), and Europe (5). A number of the representatives selected are members of our Society, and Dr. F. J. Brady, our President for next year, is the representative for North America. The Interim Committee is to be requested to explore the possibility of the formation of an International Association for Tropical Medicine and to submit concrete proposals to the Sixth International Congresses on Tropical Medicine and Malaria. Finally, there was a resolution adopted to accept the invitation of the Government of Portugal to hold the Sixth Congresses in Lisbon.

These various reports were accepted as read.

Election of Officers and Councilors for 1954

The Nominating Committee composed of Willard H. Wright, Chairman, William W. Frye, and John M. Henderson submitted a slate, which was mailed with a ballot to all active members of the Society. The votes were tabulated by the tellers, Geoffrey M. Jeffery and Kenneth D. Quarterman, appointed by the President.

The results of the election were as follows:

President-Elect	William H. Taliaferro
Vice-President	Lloyd E. Rozeboom
Councilors	Albert B. Sabin
	James J. Sapero

Committee Appointments by the President and Council

In addition to the appointments of auditors and tellers for this meeting, the President appointed the Resolutions Committee. The latter consisted of J. A. Scott, Chairman, D. E. Eyles, and D. A. Berberian.

The Council elected Leon H. Schmidt to serve on the Baily K. Ashford Award Committee during 1954, 1956, and 1958. W. A. Sodeman was elected to serve on the Walter Reed Medal Committee (composed of Past-Presidents) during 1955, 1957, and 1959. Finally, the Council elected the following members to serve on

the Nominating Committee for 1954: Paul F. Russell, Chairman, Lawrence B. Hall, and Herbert G. Johnstone.

New Business

W. V. King. As provided in the Constitution, W. V. King was transferred from active to emeritus membership.

Additional awards. A recommendation that additional awards be sponsored by the Society was considered. When the discussion led to general agreement that the initiative for new awards should come from outside of the Society, this matter was tabled.

Travel expenses for Editor of the NEWS. Approval was given to a recommendation of the Editor, Lewis W. Hackett, that travel expenses to this and subsequent annual meetings be authorized for the Editor of TROPICAL MEDICINE AND HYGIENE NEWS.

Contribution to the National Society for Medical Research. After discussion of the program of this organization, a contribution of $25.00 was voted.

Back issues of THE JOURNAL OF THE NATIONAL MALARIA SOCIETY. There was agreement that immediate steps should be taken to remove these issues from storage into libraries and other places to serve a useful purpose. G. Robert Coatney was appointed Custodian and given complete authority to effect this transfer.

Inspection of headquarters hotels for the annual meetings. The Secretary-Treasurer explained the desirability of a personal inspection of a hotel prior to its final selection as headquarters. The Council recommended, when possible, the continuation of this practice by the Secretary-Treasurer and authorized the expenditure of Society funds to cover expenses involved. A sum of $60.00 was voted to reimburse the Secretary-Treasurer for an inspection made during the summer of 1953.

1954 meeting. The Secretary-Treasurer reviewed the numerous invitations received from cities wishing to serve as host to our 1954 annual meeting. Considering all factors, Memphis, Tennessee, appeared to be a very favorable site. The Secretary-Treasurer visited Memphis in early June to inspect the facilities and to discuss details with certain local members. The facilities proved to be adequate and there was assurance that several members would serve on a local committee. Thus, the Secretary-Treasurer recommended and the Council approved Memphis as the 1954 meeting site, and the dates of November 3–6 were approved. It was also voted to invite the American Society of Parasitologists to meet jointly with the Society.

Hospitality sessions. There was general agreement regarding an opinion expressed by the President that Officers and Councilors of the Society should not solicit funds for entertainment purposes. After discussion it was voted to give the local committee the responsibility for hospitality sessions with the understanding that the members, acting as individuals and not as officials of the Society, may have the option of obtaining sponsors or arranging "dutch-treat" sessions.

Ad hoc committees for 1954. The Council empowered the President to create ad hoc committees that he and the Secretary-Treasurer deem necessary.

MINUTES OF THE ANNUAL BUSINESS MEETING

The annual business meeting of the Society was held November 14 at 8:30 A. M. in the ballroom of the Brown Hotel, Louisville, Kentucky with President William A. Sodeman presiding.

The minutes of the first meeting (Galveston, Texas, November 15, 1952) were accepted as published in the JOURNAL, May, 1953.

The Secretary-Treasurer's reports were approved as read.

The Editor-in-Chief of Publications, Lewis W. Hackett, presented the JOURNAL report, which was accepted as read.

The report of the Editor of TROPICAL MEDICINE AND HYGIENE NEWS, Leon Jacobs, was accepted as read.

The report of the auditors, Paul E. Thompson and William G. Sawitz, was read. The accounts of the Treasurer and of the Editor of TROPICAL MEDICINE AND HYGIENE NEWS were found to be in order.

Reports of committees and representatives. The various reports presented at the Council meeting were summarized. Approval of these reports was voted.

The Resolutions Committee, J. A. Scott, Chairman, D. E. Eyles, and D. A. Berberian, made the following report:

I. It is requested that the Secretary of the Society be instructed to write and send resolutions of sympathy to the families of deceased active and honorary members of the American Society of Tropical Medicine and Hygiene, during the current year.

II. The officers and members of the American Society of Tropical Medicine and Hygiene have benefited by the symposia arranged for this meeting. THEREFORE BE IT RESOLVED: that the Society extend congratulations and appreciation to the organizers and participants in the symposia on "Global Interest in Tropical Medicine" and on "Diarrheal Diseases Other Than Amebiasis".

III. To Dr. Henry E. Meleney we extend this Society's sincere thanks and highest esteem for his able presentation of the 18th Annual Charles Franklin Craig Lecture, "Problems in the Control of Schistosomiasis".

IV. To the organizations and individuals who have acted as hosts of the second annual meeting of the Society.

(a) The officers and members of the American Society of Tropical Medicine and Hygiene are deeply appreciative of the assistance and hospitality extended to the Society on the occasion of the second annual meeting held in Louisville, Kentucky, November 12-14, 1953, by the University of Louisville School of Medicine. THEREFORE BE IT RESOLVED that the thanks of the Society be expressed to Dr. J. Murray Kinsman, Dean, and Dr. Philip Davison, President, and through them to the University of Louisville.

(b) The Louisville Chamber of Commerce has greatly contributed to the success of the Second Annual Meeting of the American Society of Tropical Medicine and Hygiene, held in Louisville, Kentucky, November 12-14, 1953. THEREFORE BE IT RESOLVED that the thanks and appreciation of the Officers and Members be extended to Mr. W. J. Oberlender, Manager, Convention and Visitors Division, and through him to the Louisville Chamber of Commerce.

(c) The assistance and cooperation of the members of the staff of the Brown Hotel constituted important contributions to the success of the Second Annual Meeting of the American Society of Tropical Medicine and Hygiene, November 12-14, 1953. THEREFORE BE IT

RESOLVED that the thanks of the Officers and Members of the Society be extended to Mr. Fred C. Teich, Jr., Sales and Convention Manager, and through him to the other members of the staff of the Brown Hotel.

(d) The foresight and planning of the Local Committee on Arrangements were essential contributions to the success of the Second Annual Meeting of The American Society of Tropical Medicine and Hygiene, November 12–14, 1953. THEREFORE BE IT RESOLVED that the thanks and appreciation of the Officers and Members be expressed to the Committee Chairmen, Drs. William F. Cantrell and James A. Kennedy and through them to the other members of the staff of the University of Louisville School of Medicine, who have assisted with the arrangements for the meeting.

(e) The interest and planning of the Committee for Ladies' Entertainment contributed greatly to the pleasure of the ladies attending the Second Annual Meeting of the American Society of Tropical Medicine and Hygiene, held in Louisville, Kentucky, November 12–14, 1953. THEREFORE BE IT RESOLVED that the Officers and Members of the Society express their thanks and appreciation to the Co-Chairmen, Mrs. William F. Cantrell and Mrs. James A. Kennedy, and to the other members of the committee.

(f) The arrangements of the Committee for Ladies' Entertainment sponsored by Julius Hyman and Company added greatly to the pleasure of the ladies attending the Second Annual Meeting of the American Society of Tropical Medicine and Hygiene, held in Louisville, Kentucky, November 12–14, 1953. THEREFORE BE IT RESOLVED that the thanks and appreciation of the Officers and Members of the Society be extended to Mr. L. G. Smith, Acting Manager, Product and Sales Development and through him to the Julius Hyman and Company, Shell Chemical Corporation, Denver, Colorado.

(g) The Hospitality Sessions held at the Second Annual Meeting of the American Society of Tropical Medicine and Hygiene, Louisville, Kentucky, November 12–14, 1953, were a most important contribution to the pleasure of the individual members and guests and to the success of the meeting as a whole. THEREFORE BE IT RESOLVED that the thanks and appreciation of the Officers and Members of the Society be extended to:

(1) Dr. Edward I. Salisbury, Medical Director, United Fruit Company, and through him to the United Fruit Company, host for the Hospitality Session on Wednesday, November 11th.

(2) To Mr. Kane, Vice President, and Dr. G. E. Peabody and through them to Charles Pfizer and Company, Inc., for the Hospitality Session on Thursday, November 12.

(3) To Dr. J. B. Rice and Mr. K. M. Smoot and through them to Winthrop-Stearns Inc., host for the Hospitality Session on Friday, November 13.

(h) The Commercial Exhibits at the Second Annual Meeting of the American Society of Tropical Medicine and Hygiene, Louisville, Kentucky, November 12–14, 1953, added materially to the interest of the meeting and assisted the Society in defraying the costs. THEREFORE BE IT RESOLVED that the thanks and appreciation of the Officers and Members of the Society be expressed to Mr. Charles Estill, Associate Director, the American Foundation for Tropical Medicine, through whose efforts the exhibits were obtained.

V. To the Officers and Councilors and Editors:

(a) The Officers and Councilors of the American Society of Tropical Medicine and Hygiene are to be commended for their able administration of the Society for the success of this Second Annual Meeting. THEREFORE BE IT RESOLVED that expressions of appreciation be given to them.

(b) The various committees and their chairmen are to be commended for their share in the continuing progress of the Society.

(c) The dinner on November 12, celebrating the Fiftieth Anniversary of the Founding of the American Society of Tropical Medicine has been both interesting and instructive. THEREFORE BE IT RESOLVED that the American Society of Tropical Medicine and Hygiene express its appreciation to the Anniversary Committee, Dr. L. W. Hackett, Chairman, Drs. F. J. Brady and Leon Jacobs, for arranging this event.

(d) Dr. L. W. Hackett, Editor of the AMERICAN JOURNAL OF TROPICAL MEDICINE AND

HYGIENE is to be commended for his efforts which have resulted in a Journal of outstanding quality. THEREFORE BE IT RESOLVED that an expression of thanks of the Society be extended to him.

(e) Dr. Leon Jacobs is to be commended for editing the timely and interesting TROPICAL MEDICINE AND HYGIENE NEWS. THEREFORE BE IT RESOLVED that an expression of appreciation of the Society be extended to Dr. Jacobs.

WHEREAS, the Gorgas Memorial Laboratory was established as a living memorial to General William Crawford Gorgas in Panama, the area in which Gorgas carried out his most prolonged and important programs for the control of the two principal scourges of the Tropics, yellow fever and malaria;

WHEREAS, the Gorgas Memorial Laboratory is the only permanently established research institution in tropical and preventive medicine within the new world Tropics;

WHEREAS, this laboratory is ideally situated for expanded studies on the basic biology of diseases in the Tropics, and affords the only permanent research center where American workers in tropical biology and medicine can establish temporary or permanent headquarters for extended work on special problems;

WHEREAS, there is a continued need for practical studies of the residue of as yet unsolved problems in the diseases of the Tropics;

WHEREAS, a paper presented by the staff of the Gorgas Memorial Laboratory at these sessions emphasizes the fact that in spite of intensive investigations during the past half century, our knowledge of the epidemiology of yellow fever is incomplete;

WHEREAS, there has been an extension of jungle yellow fever from South America through Panama, Costa Rica and Nicaragua, with anticipated further invasion toward the United States through Honduras, Guatemala and Mexico, where potential vectors have been reported close to the border with the U.S.A.;

WHEREAS, this institute has demonstrated its importance as a research center in the American Tropics;

WHEREAS, after a distinguished career of a quarter of a century as Director of this Laboratory, Dr. Herbert C. Clark is presently retiring;

THEREFORE BE IT RESOLVED, that the American Society of Tropical Medicine and Hygiene, and the American Academy of Tropical Medicine hereby acknowledge the significant contribution made by this Laboratory under the direction of Dr. Herbert C. Clark;

BE IT FURTHER RESOLVED, that the two Societies strongly urge the Secretary of the Department of Health, Education and Welfare, and the Congress of the United States to increase the annual budget of the Gorgas Memorial Institute so that it may meet the requirements of its enlarged responsibilities;

BE IT FURTHER RESOLVED, that the Secretaries of these respective societies be instructed to transmit copies of this resolution to the Congress, to the Secretary of Health, Education and Welfare, and to other interested organizations and individuals, and to inform the press, and to otherwise publish this resolution to the fullest extent feasible.

WHEREAS, the experience of the 20th Century has shown that good public health in any country contributes enormously to the growth of agriculture, industry, and overseas trade and to political and social progress;

WHEREAS, the events of the past fifty years have repeatedly demonstrated the deleterious effects upon the United States of under-development and of political and social instability in other parts of the world;

WHEREAS, the national security of the United States depends to an increasing extent upon basic materials imported from under-developed and often disease-ridden tropical countries;

WHEREAS, the vastly increased volume and speed of inter-communication between the United States and the Tropics have greatly augmented the potential danger which tropical disease presents to our country;

WHEREAS, throughout the world today our country has political and defense commit-

ments which make it necessary for the United States to deploy its Armed Forces to many regions and, therefore, to maintain a practical interest in reducing the incidence of communicable disease in many overseas areas;

WHEREAS, the World Health Organization over a period of six years has conclusively demonstrated that it is a unique and effective international agency welcomed throughout the free world for its help in stimulating, coordinating, and assisting the development of public health and the control of communicable diseases;

WHEREAS, there is no doubt that the United States is materially and politically deriving great benefit from the success of the World Health Organization in developing public health in many countries with which we trade, in accelerating the control of such tropical diseases as malaria, and in lessening the chance of an invasion of the United States by disease-producing parasites;

WHEREAS, the ceiling of $3,000,000 per year fixed by the Congress as the total amount our country may contribute, does not now permit a logical expansion of WHO's activities required by its increased responsibilities;

THEREFORE BE IT RESOLVED, that the American Academy of Tropical Medicine and the American Society of Tropical Medicine and Hygiene urge the Congress of the United States to raise the statutory limitation placed upon our financial participation in WHO;

AND FURTHER, that the Secretaries of these respective organizations be instructed to transmit copies of this resolution to the Congress and to other interested organizations and individuals and to inform the press about and to otherwise publicize this resolution to the fullest extent feasible.

This report was approved as read.

The results of the election of Officers and Councilors by mail ballot were given. William H. Taliaferro was elected President-Elect of the Society for 1954, Lloyd E. Rozeboom was elected Vice-President, and Albert B. Sabin and James J. Sapero were elected Councilors for a term of four years.

It was announced that the Council elected Leon H. Schmidt to serve on the Bailey K. Ashford Award Committee during 1954, 1956, and 1958, and that William A. Sodeman was elected to serve on the Walter Reed Medal Committee during 1955, 1957, and 1959. Finally, the appointment of a Nominating Committee for 1954 was announced as follows: Paul F. Russell, Chairman, Lawrence B. Hall, and Herbert G. Johnstone.

New Business: Dr. Henry E. Meleney, retiring President of the Academy, was granted permission to read a resolution passed by the Academy approving the principle of amalgamation with the Society and inviting the Council of the Society to collaborate in formulating the mechanism of amalgamation.

It was announced that the Council had voted a $25.00 contribution to be sent to the National Society of Medical Research.

Finally, it was announced that the Council had accepted the invitation of the University of Tennessee and the Memphis Chamber of Commerce to hold the next annual meeting in Memphis, Tennessee. The meeting will be held November 3–6, 1954, and the American Society of Parasitologists will be invited to meet with us.

Respectfully submitted for publication,
JOHN E. LARSH, JR.
Secretary-Treasurer

SCIENTIFIC SESSIONS

A total of six half-day sessions was held, four for the presentation of papers and two for symposia. All sessions were held in the Ballroom of the Brown Hotel.

The first two scientific sessions were held during the first day of the meeting, Thursday, November 12, 1953. President William A. Sodeman presided over both sessions.

9:00 A.M., November 12

1. THE —EIGHTEENTH ANNUAL CHARLES FRANKLIN CRAIG LECTURE: *Problems in the Control of Schistosomiasis.* (30 mins.) HENRY E. MELENEY, School of Medicine Louisiana State University, New Orleans, La.

*2. *Bancroftian Filariasis in Costa Rica.* (10 mins.) WILLIAM H. W. KOMP, National Institutes of Health, Bethesda, Md.

3. *Eosinophilia in* Capillaria hepatica *Infection Diagnosed Antemortem. A Case Report.* (10 mins.) GILBERT F. OTTO, The Johns Hopkins University, School of Hygiene and Public Health, Baltimore, Md. and Abbott Laboratories, North Chicago, Ill.

4. *Comparative Experiments With Different Strains of* Litomosoides carinii *in Eastern and Texas Cotton Rats.* (10 mins.) J. ALLEN SCOTT and ETTA MAE MACDONALD, Medical Branch, The University of Texas, Galveston, Tex.

5. *A Histopathologic Study of the Anterior Small Intestine of Immunized and Non-Immunized Mice Infected With* Trichinella spiralis. (10 mins.) JOHN E. LARSH, JR. and GEORGE J. RACE, School of Public Health, University of North Carolina, Chapel Hill, N. C. and School of Medicine, Duke University, Durham, N. C.

6. *Treatment of Ascariasis in Honduras.* (10 mins.) MARK T. HOEKENGA, La Lima Hospital, La Lima, Honduras, C. A.

7. *The Prevalence of Helminths in Children of School Age From Rural Areas of Cambodia, Laos, and Vietnam.* (10 mins.) JOHN W. MCDOWELL, Mutual Security Agency, Special Technical and Economic Mission, Saigon, Vietnam.

8. *Adsorption of Polysaccharides Isolated From Animal Parasites onto Human Erythrocytes.* (10 mins.) JOSE OLIVER-GONZALEZ, School of Medicine, San Juan, Puerto Rico.

9. *Chemotherapy of Experimental Schistosomiasis. The Synergistic Action of Drugs in the Treatment of Schistosomiasis.* (10 mins.) D. A. BERBERIAN, E. W. DENNIS, and H. W. FREELE, Sterling-Winthrop Research Institute, Rensselaer, N. Y.

*10. *Molluscicide Operations in an Endemic Area of Schistosomiasis in the Dominican Republic.* (10 mins.) CHARLES M. VAUGHN, Department of Zoology, University of South Dakota, Vermillion, S. D., LOUIS OLIVIER, National Institutes of Health, Bethesda, Md., JAMES R. HENDRICKS, School of Public Health, University of North Carolina, Chapel Hill, N. C. and THOMAS T. MACKIE, The American Foundation for Tropical Medicine, New York, N. Y.

11. *The Effects of Temperature and Light on Reproduction and Mortality of* Oncomelania nosophora. (10 mins.) EDWARD D. WAGNER, LOIS W. WONG, and CHESTER WONG, School of Tropical and Preventive Medicine, College of Medical Evangelists, Loma Linda, Calif.

12. *Chemotherapy of Experimental Schistosomiasis. Procedures for the Screening of Drugs.* (10 mins.) D. A. BERBERIAN, E. W. DENNIS, and H. W. FREELE, Sterling-Winthrop Research Institute, Rensselaer, N. Y.

13. *Chemotherapy of Experimental Schistosomiasis. The Evaluation of Four New Thiazanthones.* (10 mins.) E. W. DENNIS, D. A. BERBERIAN, and H. W. FREELE, Sterling-Winthrop Research Institute, Rensselaer, N. Y.

* Read by title.

2:00 P.M., November 12

*1. *Treatment of Tapeworm Infestation With Quinacrine and Priodax.* HOWARD B. SHOOKHOFF, City of New York Health Department, New York, N. Y.

2. *Some Observations on Intestinal Parasites in Egyptian Villages.* ASA C. CHANDLER, Rice Institute, Houston, Texas and Faud I Research Institute for Tropical Diseases, Cairo, Egypt.

3. *A Comparison of Preservatives for Stool Specimens.* ROBERT E. RINEHART AND HELEN MARCUS, The Rinehart Foundation, Wheeler, Ore. and The University of Oregon Medical School, Portland, Ore.

4. *Further Observations of the Morphological Variations in* Trichomonas vaginalis *by Using Both Phase Contrast and Electron Microscopes.* SHOZO INOKI and YOSHIO HAMADA (Introduced by M. C. MCCOWEN), Research Institute for Microbial Diseases, Osaka University, Osaka, Japan.

5. *Prostatic Complications in Intestinal Amoebiasis.* EDGAR J. MARTIN, Oshawa General Hospital, Oshawa, Ontario, Canada.

6. *The Role of Folic Acid and Related Compounds in the Cultivation of* Entamoeba histolytica. QUENTIN M. GEIMAN and CHARLES E. BECKER, School of Public Health, Harvard University, Boston, Mass.

7. *Observations on the Virulence of* Endamoeba histolytica *During Prolonged Subcultivation.* PAUL E. THOMPSON, DUNCAN MCCARTHY and J. W. REINERTSON, Parke, Davis and Company, Detroit, Mich.

8. *The Effect of Certain Drugs on the Ability of* Endamoeba histolytica *to Ingest Red Blood Cells.* JAMES G. SHAFFER and THEODORE BALSAM, The Chicago Medical School, Chicago, Ill.

9. *Use of Fluorescein-tagged Antibody to Identify Cultures of* Endamoeba histolytica *and* Endamoeba coli. MORRIS GOLDMAN (Introduced by A. W. DONALDSON), Communicable Disease Center, Atlanta, Ga.

*10. *A Nuclear and Chromatoidal Stain for* Endamoeba histolytica. MORRIS GRODSKY and NATHAN ENTNER (Introduced by H. H. ANDERSON), School of Medicine, University of California, San Francisco, Calif.

11. *Amebicidal Activity of a Series of Synthetic Diamines.* MAX C. MCCOWEN, MAURICE E. CALLENDER, THEODORE RENNELL and JOHN F. LAWLIS, JR., Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Ind.

12. *The Chemotherapeutic Properties of Win 5047, a New Synthetic Amebacide.* E. W. DENNIS and D. A. BERBERIAN, The Sterling-Winthrop Research Institute, Rensselaer, N. Y.

13. *Antibiotic Synergism in Amebiasis.* HAMILTON H. ANDERSON, THOMAS NELSON, ARSENY HRENOFF and CHARLES FISH, School of Medicine, University of California, San Francisco, Calif. and Sonoma State Home, Eldridge, Calif.

*14. *The Role of Glucose in the Metabolism of* Entamoeba histolytica. JAMES N. DE LAMATER, University of Southern California, Los Angeles, Calif.

The third and fourth scientific scientific sessions were held during the second day of the meeting, Friday, November 13, 1953. The third, a morning session for the presentation of papers, was presided over by President William A. Sodeman. The fourth, an afternoon session devoted to a symposium sponsored by the Academy, was presided over by the Vice-President of the Academy, George R. Callender, who also served as Moderator.

9:00 A.M., November 13

1. *Demonstration of* Endamoeba histolytica *in the Liver of Guinea Pigs by Cultural Methods.* CHARLES W. REES, D. JANE TAYLOR and LUCY V. REARDON, National Institutes of Health, Bethesda, Md.

*2. *The Effect of Steroids on the Mechanism*

* Read by title.

of Resistance to Trypanosoma cruzi *Infection in Mice.* HARRY SENECA, College of Physicians and Surgeons, Columbia University, New York, N. Y.

3. *Visceral Leishmaniasis in the Hamster —Route of Inoculation, Size of Inoculum and Suspending Medium on the Course of Infection.* LESLIE A. STAUBER, Rutgers University, New Brunswick, N. J.
4. *The Cellular Reactions to Infections With* Plasmodium berghei *in the White Mouse.* IRA SINGER, University of Chicago, Chicago, Ill. and The Christ Hospital Institute of Medical Research, Cincinnati, Ohio.
5. *The Chemotherapeutic Action of Various Chemical Compounds on Acute Experimental Mouse Toxoplasmosis.* DON E. EYLES and NELL COLEMAN, National Institutes of Health, Memphis, Tenn.
6. *The Serological Epidemiology of Toxoplasmosis.* HARRY A. FELDMAN and LOUISE T. MILLER, Medical College, State University of New York, Syracuse, N. Y.
7. *Some Recent Studies in Brazilian Pemphigus.* LEON GOLDMAN, JOAO PAULO VIEIRA and MARIO FONZARI, College of Medicine, University of Cincinnati, Cincinnati, Ohio and Instituto Adhemar de Barros, Servico Do Penfigo Foliaceo, Sao Paulo, Brazil.

**8. *In Vitro Testing for Leptospiricidal Drugs.* V. T. SCHUHARDT and L. S. KUHNLEY, The University of Texas, Austin, Texas.

9. *Murine Typhus Fever Surveillance in the United States, 1952–1953.* ROY F. FRITZ, Communicable Disease Center, Atlanta, Ga.
10. *The Transmission of Dengue by* Aedes polynesiensis *Marks.* LEON ROSEN, National Institutes of Health, Bethesda, Md., LLOYD E. ROZEBOOM, School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, Md., BENJAMIN H. SWEET and A. B. SABIN, The Children's Hospital Research Foundation, Cincinnati, Ohio.
11. *Production of Dengue Vaccine Free of Paralytogenic Properties for Monkeys.* ALBERT B. SABIN and BENJAMIN H. SWEET, The Children's Hospital Research Foundation, College of Medicine University of Cincinnati, Cincinnati, Ohio.

*12. *Successful Transmissions of Western Equine Encephalomyelitis (Strain F 199) to Chickens With* Aedes sticticus *Meigen,* Mansonia perturbans *Walker, and Other Mosquitoes.* J. S. CASS (Introduced by JOHN E. LARSH, JR.), University of Minnesota, St. Paul, Minn. and College of Medicine, University of Cincinnati, Cincinnati, Ohio.

13. *Some Ecological Aspects Affecting the Dissemination of Shigella Organisms by House Flies.* THOMAS W. HAINES, Communicable Disease Center, Thomasville, Ga.

*14. *Treatment of* G. lamblia *Infections With Quinacrine and Other Antimalarials.* HOWARD B. SHOOKHOFF, City of New York Health Department, New York, N. Y.

*15. *A Clinical Evaluation of Intravenous Coconut Water Administration Based on 100 Clinical Infusions.* BEN EISEMAN, School of Medicine, Washington University, St. Louis, Mo. and the Veterans Administration, Denver, Colo., RAMIRO H. LOZANO, Tela Railroad Hospital, Tela, Honduras, C. A., and TED HAGER.

16. *Intestinal Protozoa, Helminths and Bacteria in Tahiti, French Oceania.* JOHN F. KESSEL, MARGARET PARRISH and GLENN PARRISH, School of Medicine, University of California, Los Angeles, Calif. and Institut de Recherches Medicales de l'Oceanie Francaise, Papeete, Tahiti.

** Read by A. C. Chandler.

* Read by title.

2:00 P.M., November 13

SYMPOSIUM

Global Interest in Tropical Medicine

1. *Political Implications of Global Tropical Medicine.* FRANK P. CORRIGAN, United States Mission, United Nations, New York, N. Y.
2. *Economic Interests in Global Tropical Medicine.* STACY MAY, New York, N. Y.
3. *The Military Aspect of Global Tropical Medicine.* THOMAS R. PHILLIPS, Washington, D. C.
4. *Cultural Consideration in Global Tropical Medicine.* JACQUES MAY, American Geographical Society, New York, N. Y.

The fifth and sixth scientific sessions were held during the last day of the meeting, Saturday, November 14, 1953. The fifth, a morning session devoted to a symposium sponsored by the Society, was presided over by Lloyd E. Rozeboom who introduced the Moderator, James Watt. The sixth and final meeting was an afternoon session for the presentation of papers. President-Elect Frederick J. Brady presided.

9:30 A.M., November 14

SYMPOSIUM

Diarrheal Diseases Other Than Amebiasis

1. *Shigellosis—Epidemiology in an Area of Low Incidence.* WILLIAM H. STEWART, United States Public Health Service, Thomasville, Ga.
2. *Salmonellosis—The Role of Food Processing Plants in the Dissemination of Salmonella.* ALBERT V. HARDY, Florida State Board of Health, Jacksonville, Fla.
3. *The Clinical Significance of Bacteria in the Coliform Paracolon, Pseudomonas, and Similar Groups.* MYRON E. WEGMAN, Pan-American Sanitary Bureau, Washington, D. C.
4. *The Non-amebic Non-bacillary Diarrheal Disorders.* IRVING J. GORDON, New York State Department of Health, Albany, N. Y.

2:00 P.M., November 14

1. *Motion Picture Studies of the Mosquito Stages of* Plasmodium falciparum. M. S. FERGUSON, Communicable Disease Center, Atlanta, Ga. and G. B. WOLCOTT and M. D. YOUNG, National Institutes of Health, Columbia, S. C.
2. *Infectivity to Mosquitoes of* Plasmodium falciparum *Infections Throughout the Course of Infection in the Human Host.* GEOFFREY M. JEFFERY, National Institutes of Health, Milledgeville, Ga. and DON E. EYLES, National Institutes of Health, Memphis, Tenn.
3. *An Outbreak of Malaria in California.* ROSEMARY BRUNETTI, California State Department of Public Health, Berkeley, Calif. and ROY F. FRITZ, Communicable Disease Center, Atlanta, Ga.
4. *The Six-Year Philippine-American Plan for Malaria Control in the Philippines.* ANTONIO EJERCITO, Philippine Department of Health, Manila, Philippines, A. D. HESS and AUBREY L. WILLARD, Foreign Operations Administration, Manila, Philippines.
5. *The Role of Insecticides in the Malaria Control Program of the Tennessee Valley Authority.* F. E. GARTRELL and G. F. LUDVIK, Tennessee Valley Authority, Chattanooga, Tenn.

*6. *Infrared Spectrophotometry as a Means for Identification of Mosquitoes.* ALBERT A. BENEDICT and DON W. MICKS,

* Read by title.

Medical Branch, University of Texas, Galveston, Texas.

7. *Insects of Public Health Significance Originating in Reservoirs of the Tennessee Valley Authority.* W. E. Snow and Eugene Pickard (Introduced by F. E. Gartrell), Tennessee Valley Authority Chattanooga, Tenn.
8. *New Information on Sylvan Yellow Fever and Its Possible Vectors in Middle America.* Harold Trapido and Pedro Galindo, Gorgas Memorial Laboratory, Panama, R. de P., Jorge Boshell, Pan American Sanitary Bureau, Guatemala City, Guatemala.
9. *Recent Improvements in Equipment for the Application of Residual Insecticides.* Lawrence B. Hall and Kenneth D. Quarterman, Communicable Disease Center, Savannah, Ga.
10. *Fly Production in Urban, Suburban, and Rural Privies in Southeastern Georgia.* John W. Kilpatrick, Herbert F. Schoof and Kenneth D. Quarterman, Communicable Disease Center, Savannah, Ga.
11. *The Control of Fly Populations in Rural Areas of Southeastern Georgia With Parathion Impregnated Cords.* John W. Kilpatrick and Wayland J. Hayes, Jr., Communicable Disease Center, Savannah, Ga.
12. *The Occurrence and Movement of* Periplaneta americana *(L) Within an Urban Sewerage System.* Herbert F. Schoof and Russell E. Siverly, Communicable Disease Center, Savannah, Ga.
13. *Single Dose Treatment of Malaria in Honduras,* Mark T. Hoekenga, La Lima Hospital, La Lima, Honduras, C. A.
14. *Malaria Surveillance in the United States, 1953.* Roy F. Fritz, Communicable Center, Atlanta, Ga.

SCIENTIFIC EXHIBITS

The following exhibits were displayed in the South Room of the Brown Hotel.

"The Ectopic Development of Oocysts of Malaria in Mosquitoes." A. B. Weathersby, Naval Medical Research Institute, National Naval Medical Center, Bethesda, Md.

"Malaria Control by Drugs Given Once Monthly." A. J. Walker and T. Wilson, Tulane University School of Medicine, New Orleans, La., and Institute for Medical Research, Kuala Lumpur, Malaya.

SPECIAL EVENTS

Highlights of the meeting included a tour of The University of Louisville School of Medicine, a dinner commemorating the fiftieth anniversary of the founding of The American Society of Tropical Medicine (one of the parent organizations of the present Society), the presentation of the Theobald Smith Medal to R. E. Dyer (by A. C. Chandler), the presentation of the Walter Reed Medal to L. W. Hackett (by H. H. Anderson for J. S. Simmons), the presentation of the Charles Franklin Craig Lecture by H. E. Meleney, and the joint dinner session of the Society and the Academy. A. B. Sabin presided at the dinner session, which included the Presidential Addresses of the Society (W. A. Sodeman: *Our Future?*), and the Academy (H. E. Meleney: *Unfinished Business in Tropical Medicine*). For more details of these events, see Tropical Medicine and Hygiene News, December, 1953.

MINUTES OF THE TWENTIETH ANNUAL BUSINESS MEETING OF THE AMERICAN ACADEMY OF TROPICAL MEDICINE

The twentieth annual meeting of the Academy was held jointly with the American Society of Tropical Medicine and Hygiene at the Brown Hotel, Louisville, Kentucky, November 12 to 14, 1953.

On the afternoon of Friday, November the 13th, a general session was held in the Ball Room of the Brown Hotel at which Vice-President George R. Callender presided. The presentation of the Theobald Smith Medal of the American Academy of Tropical Medicine was made by Dr. Asa C. Chandler to Dr. R. E. Dyer. This was followed by a Symposium entitled "Global Interest in Tropical Medicine". Four splendid presentations were made by: (1) Dr. Frank P. Corrigan, United States Mission, United Nations, New York, N. Y., "Political Implications of Global Tropical Medicine", (2) Dr. Stacy May, Rockefeller Brothers Fund, Inc., New York, N.Y., "Economic Interests in Global Tropical Medicine", (3) Brig. Gen. Thomas R. Phillips, Washington, D. C., "The Military Aspect of Global Tropical Medicine", (4) Dr. Jacques May, American Geographical Society, New York, N. Y., "Cultural Consideration in Global Tropical Medicine".

The twentieth annual dinner of the Academy was held jointly with the American Society of Tropical Medicine and Hygiene in the Ball Room of the Brown Hotel at 7:00 p.m., November the 13th. Dr. Albert B. Sabin acted as Toastmaster and Presidential Addresses were given by Dr. William A. Sodeman of the American Society of Tropical Medicine and Hygiene on "Our Future?" and by Dr. Henry E. Meleney on "Unfinished Business in Tropical Medicine".

The business session of the Academy was held in the Louis XVI Room immediately following the adjournment of the dinner meeting. Those in attendance were: H. E. Meleney (presiding), H. H. Anderson, F. J. Brady, G. R. Callender, A. C. Chandler, H. C. Clark, G. R. Coatney, W. W. Cort, R. E. Dyer, E. C. Faust, Q. M. Geiman, L. W. Hackett, E. H. Hinman, H. S. Johnstone, J. F. Kessel, J. Oliver-Gonzalez, G. F. Otto, L. E. Rozeboom, P. F. Russell, E. J. Salisbury, J. J. Sapero, J. A. Scott, G. C. Shattuck, W. A. Sodeman, F. L. Soper, G. K. Strode, R. B. Watson.

The meeting was called to order by President Meleney and the minutes of the Nineteenth Annual Meeting, which had been published, were approved. An announcement was made of the vote on the Constitutional Amendment of the By-Laws, Section 5. *Election to Membership, Honorary Membership and Emeritus Membership*—"Upon nomination for membership or honorary membership by the Council, a majority of the ballots cast by members, by written proxy or in person, at an annual meeting shall be necessary for election; provided that not more than ten (10) candidates receive a majority vote each year or that the total membership does not exceed one hundred (100). In the event the annual quota or the membership limits as stated in the preceding paragraph are ex-

ceeded, eligible places shall be filled by candidates receiving the largest number of votes."

Forty-six votes were received by mail with only two in opposition. The President declared the Constitutional Amendment adopted.

The announcement of the tellers' count of ballots in the election of new officers was made and the following slate which had been nominated by the Council was approved.

For President—Brig. Gen. George R. Callender
For Vice-President—Capt. James J. Sapero
For Secretary—Dr. E. Harold Hinman
For Treasurer—Dr. J. M. Andrews
For Councillor (five-year term)—Dr. Q. M. Geiman

The following five individuals having received the highest number of votes were declared elected as new members: Drs. Eloise B. Cram, John E. Larsh, Edwin H. Lennette, Donald B. McMullen, Albert B. Sabin.

The Academy also unanimously voted to transfer to Emeritus Membership Dr. W. V. King. The resignation of Dr. L. R. Cleveland was accepted.

The Secretary gave his Ad Interim Report which included a summary of the membership status, correspondence with officers and members of the Council during the year, the arrangement of the Symposium, the action of the Theobald Smith Medal Committee, and the recommendation of appropriate resolutions with respect to the death of our Emeritus and Charter member Dr. Marshall A. Barber and Emeritus member Dr. E. L. Walker. The Secretary's Report was accepted and he was instructed to prepare appropriate resolutions concerning the death of the Emeritus members and to the individuals responsible for the provision of the splendid facilities for the Annual Meeting.

In the absence of the Treasurer the Secretary presented a summary of the Treasurer's Report which had previously been audited by Dr. H. W. Brown and Dr. Hamilton H. Anderson and found correct. This report was accepted and the Treasurer instructed to make the usual $100 appropriation for secretarial help to the Secretary and $50 for the operation of the Secretary's office and a grant of $25 to the National Society for Medical Research.

It was voted to assess members $3.00 dues for 1954.

FUTURE OF THE ACADEMY

At the last Annual Meeting the retiring President of the Academy appointed a Committee of five composed of: Dr. G. F. Otto, Chairman, Dr. W. A. Sodeman, Dr. F. J. Brady, Dr. G. K. Strode and Dr. W. H. Wright, to study the status of the Academy and to report their recommendations at the next Annual Meeting. Subsequently the American Society of Tropical Medicine and Hygiene appointed an Academy Liaison Committee consisting of Drs. W. Clark Cooper, Archie D. Hess, Donald B. McMullen, Thomas H. Weller and Albert B. Sabin, Chairman. All of these individuals were non-members of the American Academy of Tropical Medicine. The attitude of these two committees towards the future of the Academy formed the principal topic of discussion of the Annual Luncheon of

the Officers and Councillors of the Academy. As a result of this discussion it was agreed to present to the business meeting of the Academy a resolution approving the principle of amalgamation with the American Society of Tropical Medicine and Hygiene. After a thorough discussion of the future of the Academy the following resolutions was unanimously adopted and signed by the 24 members of the Academy who were in attendance at the Annual Business Meeting at the time of the introduction of the resolution:

"Whereas, the importance of tropical medicine to the United States of America is greater today than at any time previously in its history because of current defense commitments in tropical lands, because of increasing dependence on basic metals or other strategic materials from tropical areas, because of the importance of an expanding export trade with tropical countries and because of the need to assist the development of tropical peoples in the interests of international peace and stability;

Whereas, the American Society of Tropical Medicine and Hygiene has now become a large and effective organization whose membership embraces all aspects of the study, treatment, and control of tropical diseases;

Whereas, the American Academy of Tropical Medicine believes there is strength in unity and that by combining its forces with those of the American Society of Tropical Medicine and Hygiene it can now more effectively carry out its original mandate;

Therefore, be it resolved that the Academy approve the principle of amalgamation with the American Society of Tropical Medicine and Hygiene and instruct its Council to invite the Council of the American Society of Tropical Medicine and Hygiene to collaborate in working out the mechanism of amalgamation."

OTHER BUSINESS

The proposal for an International Association of Tropical Medicine was reported upon by Drs. Brady and Soper. The decision reached at the Istambul Congresses of Tropical Medicine and Hygiene was that no permanent society should be formed but that the Interim Committee could perform the necessary activities between International Congresses. Dr. Paul F. Russell presented a brief report on the International Congresses at Istambul.

At the close of the business session President-Elect George R. Callender was inducted into office.

The meeting ajourned at 11:45 p.m.

E. Harold Hinman, M.D.
Secretary

BOOKS RECEIVED

Leprosy. A Survey of Recent Legislation. Reprint from the International Digest of Health Legislation, 1954, **5**: 3-36. 35 pp. WHO. Distributed by Columbia University Press, International Documents Service, 2960 Broadway, New York 27, N. Y. 1954. Price $.25, 1/9, Sw.Fr. 1.-

The Dynamics of Virus and Rickettsial Infections. International Symposium. (Sponsored by Henry Ford Hospital, Detroit, Oct. 21-23, 1953.) ed. Frank W. Hartman, Frank L. Horsfall, Jr., John G. Kidd. 461 pp., illustrated. New York, The Blakiston Co., 1954. Price $7.50.

Plague, by R. Pollitzer (formerly of the Division of Epidemiological and Health Statistical Services, WHO). 698 pp., illustrated, with 2 in color. Bibliographies. WHO Monograph Series No. 22. Distributed by Columbia University Press, International Documents Service, 2960 Broadway, New York 27, N. Y. 1954. Price, clothbound $10.00, 3/5, Sw.fr. 40; paperbound $9.00, 3/0, Sw.fr. 36. French ed. in preparation.

Amebiasis. American Lecture Series No. 191. A monograph in American Lectures in Internal Medicine, by Ernest Carroll Faust, Head of the Division of Parasitology, Department of Tropical Medicine and Public Health, Tulane University, New Orleans, Louisiana. 154 pp., illustrated, with one plate in color. Springfield, Illinois, Charles C. Thomas. 1954. Price $4.75. Published simultaneously by Blackwell, Ltd., Oxford, England, and the Ryerson Press, Toronto, Canada.

Estado Inmunitario Entozoosico. Estudio experimental y crítico sobre la reacción humoral, comprobada especialmente en las parasitosis intestinales, hidatidosis y sífilis por medio de los antígenos de *Tenia*, by Gustavo A. Rosas-Costa, Head of the Bacteriological Institute of the Province of Entre Rios, Argentina. 116 pp. Buenos Aires, Imprenta Ferrari Hermanos. 1947.

Biologisch-Medizinisches Taschenjahrbuch, by Dr. Hans Haferkamp. 14th year, 580 pp. Stuttgart, Hippokrates-Verlag Marquardt & Cie. 1954. Price DM 7.50.

Manual of Clinical Mycology, by Norman F. Conant, Ph.D., David T. Smith, M.D., Robert D. Baker, M.D., Jasper L. Callaway, M.D., Duke University School of Medicine; and Donald S. Martin, M.D., Communicable Disease Center, Chamblee, Georgia. 2nd edition, 456 pp., with 202 figures. Philadelphia and London, W. B. Saunders Co. 1954. Price $6.50.

Wine as Food and Medicine, by Salvatore P. Lucia, M.D., Professor of Medicine, University of California School of Medicine. 149 pp. New York, The Blakiston Company, Inc. 1954. Price $3.00.

Map of World Distribution of Rickettsial Diseases, Tick-borne and Mite-borne Forms (No. 11 of the series in preparation of an Atlas of Diseases) by Department of Medical Geography, American Geographical Society. New York, American Geographical Society. 1954. Price $1.25 folded, $1.50 flat.

BOOK REVIEWS

The Conquest of Plague. A study of the evolution of epidemiology, by L. Fabian Hirst, M.D. Lond., with a foreword by Lieut.-Gen. Sir William Macarthur. 478 pp. with illustrations and maps. New York: Oxford University Press, 114 Fifth Avenue, 1953. Price $11.00.

As stated in the preface of this well-written work, it purports to be neither a history of plague epidemics nor a systematic textbook, but represents "a study of the development of human beliefs about the origin of the malady from the era of primitive man to the present day". Hence Hirst's book, though conveying well-assembled information to those who are familiar with the problems of epidemiology, can—as the author himself admits—serve only

as a general introduction to the study of plague for young investigators. Indeed, one cannot help feeling that some sections devoted to the present state of knowledge on plague ecology and control are all too short. It must be noted as well that some of the opinions vigorously propounded by the author are not shared by other modern plague workers. For instance, Hirst maintains that the existing international sanitary regulations for plague quarantine are insufficient because they pay no attention to the long-distance transport of infected rat fleas which, though separated from their hosts, are able to survive in ship-borne merchandise. However, the actual evidence adduced in the past to prove a prolonged survival of such fleas in the cargoes has not been considered as convincing by most other plague workers, and their opinion has been strongly supported by the results of investigations recently carried out under the auspices of the United States Public Health Service (Norris *et al.*, 1953).

However, as noted above, in spite of this and of other objections Hirst's book, because it furnishes an interesting background for their actual work, will prove stimulating for plague workers and epidemiologists in general.

K. F. MEYER

Global Epidemiology. A geography of disease and sanitation. Volume 3. The Near and Middle East, by JAMES STEVENS SIMMONS, Dean, Harvard University School of Public Health; TOM F. WHAYNE, Colonel, M.C., United States Army; GAYLORD W. ANDERSON, Director, School of Public Health, University of Minnesota; HAROLD MACLACHLAN HORACK, Instructor, Tulane University School of Medicine. Associate Author, RUTH ALIDA THOMAS, and collaborators. 357 pp., New York, J. B. Lippincott Co., 1954. Price $12.00.

This volume on Global Epidemiology, is the third of a series which covers the region generally known as the Near and Middle East. Countries or dependencies covered include Cyprus, Iraq, Israel, Jordan, Lebanon, Syria, Afghanistan, Iran, Turkey, Aden, Bahrain, Kuwait, Muscat and Oman, Qatar, Saudi Arabia, Trucial Oman, Yemen. In other words, the approaches to Eastern Asia and Europe, as well as the Arabian Peninsula are included.

This is truly a monumental task, since so little is known of so many parts of this vast area. Unfortunately, national boundaries are not barriers to the spread of disease by the Bedouin in the desert so that the divisions by national boundaries are totally artificial in most cases.

Not only is geography and climate covered, but population (where known) and socio-economic conditions, environment and sanitation, health services and medical facilities, and diseases reported by various means, and a summary and bibliography comprise each country's report. Unfortunately, while medical care and education is of a high order in such a country as Lebanon, it is truly an oasis in a health vacuum which largely dominates the Arabian peninsula, and the Syrian, Iraq, and Iranian desert areas.

One may get the impression that the many authorities cited give substance to the disease incidence and other health factors reported in this volume. However, many of these reports are spot surveys only and many are either unconfirmed or lacking in details which are generally considered adequate.

It would be difficult to find the data collected in this volume in any other single reference.

HAMILTON H. ANDERSON

Expert Committee on Plague, Second Report. WHO Technical Report Series No. 74. 13 pp. Available also in French edition. WHO, Geneva, 1953. Distributed by Columbia University Press, International Documents Service, 2960 Broadway, New York 27, New York. Price $.10, 9 d., Fr.fr. 30.00, Sw. Fr. 0.40.

Recent scientific advances have greatly increased the available means of plague control. The sulfonamides and antibiotics, new rodenticides, and more effective pulicides have led to rapid progress in the treatment and the prevention of this disease, in the protection of contacts, in the extermination of rats, and in flea control.

The second report of the Expert Committee on Plague summarizes in concise form the results of plague-control experience in recent years. In certain regions these results have been most impressive. The report also gives an account of surveys on the role of wild rodents in the transmission of plague, enumerates the procedures for distinguishing the plague bacillus from the pseudotuberculosis bacillus, and describes the basic methods for the laboratory diagnosis of the disease.

L. W. HACKETT

Atlas of Diseases. 1. Poliomyelitis, 2. Cholera, 3. Malaria Vectors, 4. Helminthiases, 5. Dengue and Yellow Fever, 6. Plague, 7. Leprosy, 8. Study in Human Starvation, I. Sources of Selected Foods, 9. Study in Human Starvation, II. Diets and Deficiency Diseases, 10. Rickettsial Diseases, I. Mouse-borne and Flea-borne Typhus. Department of Medical Geography, American Geographical Society, New York 32, N. Y. 1952–1953. Price $1.25 each.

Ten sheets have now been published of the 25 which will make up the *Atlas of Diseases* being compiled by the Department of Medical Geography of the American Geographical Society. On each sheet a number of medical maps are plotted to show the world distribution of selected diseases and deficiencies in a compact and readable way. This census of known facts is the first step toward a study of the geographic correlations which foster the occurrence of a specific disease in a given area at a given time.

Like all maps of this sort, they cannot be entirely correct, complete, or up-to-date. This of course is mainly due to errors or inadequacies of the sources of information. Experts in the different diseases, to whom the maps were sent by this Editor, were unanimous in saying that all contain a great deal of useful information and present a very interesting and worthwhile compilation of data scattered in many different places. These maps undoubtedly are a valuable contribution and constitute a ready source of important information.

The individual sheets have elicited the following comments from the consultants, which are here given in condensed form.

Plate 1. *Poliomyelitis:* This represents a compilation of much useful data brought together from widely scattered sources. The explanatory remarks contain the necessary cautious admonitions which should prevent misleading conclusions on the part of the uninitiated. (A. B. Sabin)

Plate 2. *Cholera:* This is adequate as far as presently available information goes. It may be that material now being prepared by Dr. S. Swaroop of WHO on the history and present incidence of cholera may suggest certain emendations. (R. Pollitzer)

Plate 3. *Malaria:* This is a little out of date in a field which is undergoing such rapid evolution. This is symbolized by the citation of M. F. Boyd's 1930 "Introduction to Malariology", while his great "Malariology" published in 1949 is not referred to. *Falciparum* malaria is shown as having "average prevalence" in North Australia and the Southern United States; the map is dated 1951, when this was no longer true. Perhaps the maps should indicate rather the period of prevalence referred to. On the whole, however, the data on distribution of the disease and its vectors are quite complete and useful. (W. C. Reeves)

Plate 4. *Helminthiases:* This covers many parasite species, and in view of the unconfirmed nature of many reports, it has steered a conservative course, though some errors have crept in. For example, it is questionable whether *Dracunculus medinensis* occurs in the Americas at all, in spite of assumptions handed down in the literature; *Echinococcus granulosus* certainly occurs in Canada and the U. S., though it is rare; the distribution of *Fasciolopsis hepatica* infection in man cannot be correct since 100 cases have been reported from Cuba, but if the infection in sheep is intended, the map is out of place as is also the one on sheep distribution; the combined distribution of *Wuchereria bancrofti* and *W. malayi* is incorrect for the latter, which is confined to South India and S. E. Asia. In spite of these criticisms, this is a definite contribution to medical geography, giving at a glance a fair idea of the extent of a given problem. (D. L. Augustine)

Plate 5. *Yellow fever and Dengue:* This is an excellent job without major errors. The map

will be of great value to anyone interested in this field, and should be kept up to date as more information becomes available. (M. Theiler)

Plate 6. *Plague:* There are some omissions and errors in the maps of Asia and Europe. No indication is given of the outbreak of pneumonic plague in Manchuria in 1910–11 and 1920–21, when several urban centers were severely infected; in Central China the map shows Chekiang and Kiangsi Provinces more severely and permanently affected than Fukien, whereas the opposite is true; the easternmost and westernmost tips of Java never had plague, as shown on the map. There are also a number of additions and corrections called for in the paragraph on Epidemiology and in the Résumé of Natural History, but the maps in general give an adequate picture of the incidence of this disease during the period under review (R. Pollitzer)

Plate 7. *Leprosy:* The map agrees with the best current world references, and the elliptical equal-area projection map represents a real contribution. The paragraphs on Epidemiology are in accord with the present thinking on the subject. (E. M. Gordon)

Plate 8. *Study in Human Starvation. I. Sources of Selected Foods:* This covers an amazing amount of data and should be of value to students and investigators. The principal defect seems to be lack of population density data, which would make the maps more valuable. Only one of the three tables (percentage of total area in arable and pasture land) is directly referable to the maps; a saving of space here might result in larger maps, which are so small that overlapping areas are easily over-looked. It would make for easier reading if each map had its own legend, even though this might be common to several maps. (Agnes Fay Morgan)

Plate 9. *Study in Human Starvation. II. Diets and Deficiency Diseases:* Much of the information in the extensive bibliography is qualitative only, as is frankly stated. This might profitably be shown in the graphic portrayal, distinguishing areas that have been adequately surveyed so as to permit objective conclusions regarding diet, from those for which only qualitative data exist. The maps would then serve the additional purpose of indicating where more survey work is needed. The legend should perhaps indicate that blank areas do not mean a lack of deficiencies, but only a lack of information. The maps however represent a noble attempt to portray on the basis of admittedly insufficient data, the state of the world in regard to diets and deficiency diseases. (Ruth L. Huenemann)

Plate 10. *Rickettsial Diseases. I. Mouse-borne and Flea-borne Typhus:* The map seems accurate and should be extremely useful not only to epidemiologists but to workers in other allied fields of medicine. The list of references is well chosen and this map and the others to follow will constitute a valuable and ready source of information. (E. H. Lennette)

L. W. HACKETT

Salmonellae and Shigellae. Laboratory diagnosis correlated with clinical manifestations and epidemiology, by ALFRED J. WEIL, M.D., the Bronx Hospital, New York, AND IVAN SAPHRA, M.D., The Beth Israel Hospital, New York. 252 pp. with 29 illustrations. Chas. C Thomas, Springfield, Ill., 1953. Price $7.75.

The authors of this text have devoted prolonged study to the detailed bacteriology of "Salmonellae and Shigellae." This volume reflects their interest. About one half is devoted to a detailed definition of the genera and to the serological differentiation of groups and types. One cannot approve the nomenclature used for *Shigella*. A Commission of the International Congress of Microbiology has made recommendations concerning this. Regrettably, throughout this text, the designations and classification recommended earlier by Weil are still employed. This perpetuates a confusion which can be overcome only by accepting and following the recommendation of a responsible International Committee as virtually all other bacteriologists have done. Despite this weakness, these chapters are the superior ones in the text. There is much useful information, particularly for the mature rather than the beginning worker. There are, by contrast, only two brief and inadequate chapters on the isolation and identification of these organisms, a highly important subject for most clinical and public health laboratories. Even the brief statements are deficient in many ways. There is no mention of the use of bismuth sulphite (Wilson-Blair) agar, the most

highly efficient medium for the isolation of *S. typhi*, nor of brilliant green agar, a superior medium for most of the other *Salmonella*. The rectal swab technic is not the one which has been described and recommended. Instead of the accepted cotton tipped swab, they state, "The swabs are pieces of cellophane fitted to the end of an applicator with the help of a rubber band." The reviewer sees nothing to recommend in this modification of the described technic and it appears to be one which can not be recommended. The technics of isolation are not described in a manner helpful to the usual technical worker in a medical laboratory. The two colored plates fail to give an accurate picture of changes observed in the laboratory and detract from, rather than add to, the presentation.

The chapter on clinical features and epidemiology provides information and an outlook believed needed by bacteriologists. These data necessarily are sketchy. In one regard, the epidemiology lacks clarity. Since *S. typhi* has been brought into the broad group of *Salmonella*, the attempt has been made similarly to unify the clinical and epidemiological pictures of these infections. Actually, there is a clear and distinctive character to the epidemiological and clinical picture of typhoid and the related para-typhoid infections which differs notably from that of the *Salmonella* infections spread from lower animals to man. In the clinical and epidemiological, if not in the bacteriological field, there is merit in maintaining this differentiation. The printing in the text is excellent. Unfortunately, the same high standard was not maintained in editing and proof reading. The too numerous and obvious errors detract seriously from the value of this publication. The authors have stated fully their own preferences and views and have given a summary of the experience and practice of workers in the field. This text will have interest chiefly to those who do the detailed bacteriological studies of "Salmonellae and Shigellae." It cannot be recommended as a practical guide for bacteriologists in public health or clinical laboratories, nor is it written to be of interest to clinicians or epidemiologists.

ALBERT V. HARDY

W. H. O. Expert Committee on Leprosy, First Report. Technical Report Series No. 71. 28 pp., available also in French edition. W.H.O. Geneva, 1953. Distributed by Columbia University Press, International Documents Service, 2960 Broadway, New York 27, New York. Price $.20, 1/6, Fr. fr. 65., Sw. fr. 0.80.

This report contains the collective views of an international group of experts on the epidemiology, control, treatment, classification and immunology of leprosy. The disadvantages of compulsory isolation are stressed and the superior effectiveness of sulfone treatment over all others in nontoxic doses is emphasized. The infectivity of open and closed cases and the basic principles of control are discussed. There are many problems still to be solved and this succinct report brings us up to date on the various aspects of a disease still of great importance in many parts of the world.

L. W. HACKETT

Respiratory Diseases and Allergy. New Method of Approach, by JOSEF S. SMUL, M.D. Fellow National Gastro-Ent. Assoc., Member New York Academy of Sciences, 80 pp., New York 3, N. Y., Medical Library Co., 232 East 15 St., 1953. Price $2.75.

Dr. Smul's idea is that a whole series of names refer to the same disease—he calls it "respirallergy"—and that the treatment of all the different variations is the same and can be effected by injecting the patients with what the author calls the three universal desensitizers and by that he means ragweed, vaccine and house dust. If the patient is treated with doses of these three materials according to a schedule, he will be better.

The idea is interesting until one finds that the list of syndromes includes neurosis of the respiratory tract, hay fever, perennial rhinitis, bronchiectasis and fetid bronchitis. In these diseases the pathology varies with the location of the lesion, but the author's point is that the nature of this pathology is about the same in each case. Is our diagnostic acumen to be thrown away? Is there no use in looking at the x-ray which shows shadows characteristic of paranasal sinusitis or bronchiectasis? Are these shadows to be disregarded in advising treat-

ment? If the author means these things, his book does harm. Attempts at simplification are laudable when they do not go too far.

Section 2 of the book deals with the infectious diseases of the respiratory system. Here are 2 pages on tonsilitis, 4 on diphtheria, 2 on pertussis, 5 on influenza, 7 on pneumonia, 3 on pleurisy, 2 on infarcts and then almost 4 pages all devoted to pulmonary tuberculosis.

Section 3 on neoplastic diseases contains almost 2 pages—and the book is small, the pages are very short. What he says in these two sections is all right as far as it goes. It is a sort of primer—interesting perhaps to nurses or possibly for the patient's family but the author is quite wrong when he says in the preface: "Owing to the exclusion of many useless theories this small volume completely covers all diseases of the respiratory system." Such a book cannot be recommended.

F. M. RACKEMANN

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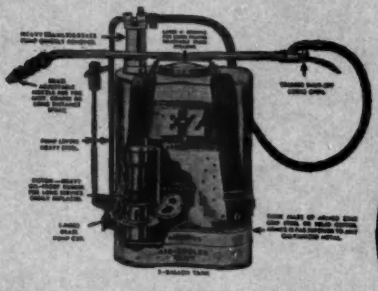

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